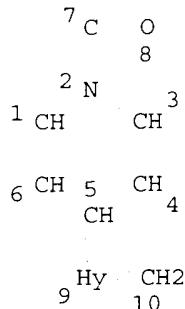


=> d 17
L7 HAS NO ANSWERS
L7 STR



NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 1
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

=> s 17 ful
FULL SEARCH INITIATED 11:11:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 403812 TO ITERATE

99.1% PROCESSED 400000 ITERATIONS 2 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.14

FULL FILE PROJECTIONS: ONLINE **INCOMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 403812 TO 403812
PROJECTED ANSWERS: 2 TO 6

L9 2 SEA SSS FUL L7

=> d 1-2

L9 ANSWER 1 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 375848-73-0 REGISTRY
CN Piperidine, 4-[5-(aminomethyl)-3-pyridinyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)
MF C25 H28 N4 O . 3 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

O

N C N

N

Ph CH₂ CH₂
CH₂ NH₂

● 3 HCl

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L9 ANSWER 2 OF 2 REGISTRY COPYRIGHT 2003 ACS
RN 375848-72-9 REGISTRY
CN Piperidine, 4-[5-(aminomethyl)-2-thienyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)
MF C24 H27 N3 O S . 2 Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

O

H₂N CH₂ S N C N

Ph CH₂ CH₂

● 2 HCl

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	153.51	153.72

FILE 'CAPLUS' ENTERED AT 11:11:51 ON 06 MAY 2003
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FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 19
L10 1 L9

=> d bib abs hitstr

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	-----	-----	-----	-----
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1296972	A1	20030402	EP 2001-930925	20010427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001011206	A	20030415	BR 2001-11206	20010427
	NO 2002005601	A	20030106	NO 2002-5601	20021121
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
	WO 2001-US13811	W	20010427		
OS	MARPAT	136:5917			
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are β . to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkylloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prep'd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-

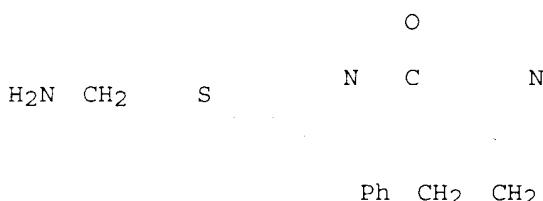
benzyloxycarbonylpiperidine (DMF, K₂CO₃, PdCl₂(dppf).bul.CH₂Cl₂, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H₂, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr₂NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

IT 375848-72-9P 375848-73-0P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

RN 375848-72-9 CAPLUS

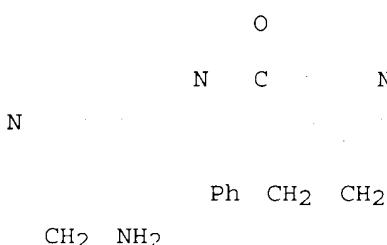
CN Piperidine, 4-[5-(aminomethyl)-2-thienyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 375848-73-0 CAPLUS

CN Piperidine, 4-[5-(aminomethyl)-3-pyridinyl]-1-[[5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)



●3 HCl

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 HAS NO ANSWERS
L8 STR

@1 2 9 12
C C C O
C 37 C 10 N 13

@6 C C C 11
C 4 8
@5

Ak N
@14 15

VPA 14-5/6/1 U

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ELEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 11 4

NUMBER OF NODES IS 15

STEREO ATTRIBUTES: NONE

=> S 18 ful
FULL SEARCH INITIATED 09:12:27 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 9223 TO ITERATE

100.0% PROCESSED 9223 ITERATIONS
SEARCH TIME: 00.00.01

8 ANSWERS

L10 8 SEA SSS FUL L8

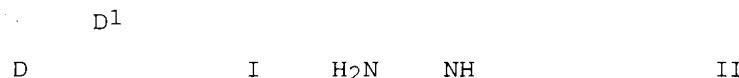
=> S 110
L11 2 L10

=> D bib abs hitstr 1-2

L11 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS
AN 1998:126233 CAPLUS
DN 128:192644
TI Preparation of amidinophenyl-pyrrolidines, -pyrrolines, and
-isoxazolidines as inhibitors of factor Xa
IN Fevig, John Matthew; Quan, Mimi Lifen
PA Du Pont Merck Pharmaceutical Company, USA
SO PCT Int. Appl., 206 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806694	A1	19980219	WO 1997-US14222	19970813
	W: AM, AU, AZ, BR, BY, CA, CN, CZ, EE, HU, IL, JP, KG, KR, KZ, LT, LV, MD, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 6057342	A	20000502	US 1997-888718	19970707
	AU 9740645	A1	19980306	AU 1997-40645	19970813
	EP 934265	A1	19990811	EP 1997-938270	19970813
	EP 934265	B1	20030102		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 20000516234	T2	20001205	JP 1998-509980	19970813
	AT 230392	E	20030115	AT 1997-938270	19970813
PRAI	US 1996-689945	A	19960816		
	US 1996-33436P	P	19961223		
	US 1996-23417P	P	19960816		
	WO 1997-US14222	W	19970813		
OS	MARPAT	128:192644			
GI					

R



AB The title compds. [I; D, D1= CN, C(:NR7)NR8R9, NHC(:NR7)NR8R9, etc.; Z = CH₂, C(O), CH₂C(O), etc.; J1, J2 = O, CH₂ (provided that if J1 = O, then J2 = CH₂ and if J2 = O, then J1 = CH₂); R = CO₂R₁, COR₁, OR₁, etc.; R_a = H, C₁₋₄ alkyl; R_b = H; when J1, J2 = CH₂, then R_a, R_b = a bond; R₁ = H, (un)substituted C₁₋₄ alkyl, C₃₋₆ carbocyclyl, etc.; A = (un)substituted C₃₋₁₃ carbocyclyl, 5-10 membered heterocyclyl; B = XY, NR₂R_{2a}, C(:NR₂)NR₂R_{2a}, etc.; X = C₁₋₄ alkylene, C(O), C(O)NR₂, etc.; Y = (un)substituted C₃₋₁₀ carbocyclyl, 5-10 membered heterocyclyl; R₂, R_{2a} =

H, C1-4 alkyl, Ph; R2R2a = (un)substituted 5-6 membered ring; R7 = H, OH, C1-6 alkyl, etc.; R8, R9 = H, C1-6 alkyl, (CH₂)_nphenyl; n = 0-3; m = 0-2] and their salts, useful as anticoagulants in treating or preventing thromboembolic disorders, were prep'd. Thus, treatment of 3-cyanobenzaldehyde with Me (triphenylphosphoranylidene)acetate followed by reacting the resulting Me trans-3-cyanocinnamate with N-benzyl-N-(trimethylsilylmethyl)aminomethyl Me ether, and HCl gas bubbling through the soln. of trans-1-benzyl-3-carbomethoxy-4-(3-cyanophenyl)pyrrolidine, and treatment of the resulting solid with (NH₄)₂CO₃ in MeOH afforded the title compd. trans-II. Some compds. I were evaluated and showed Ki of < 5 .mu.M against human thrombin.

IT 203512-01-0P 203512-02-1P 203512-09-8P

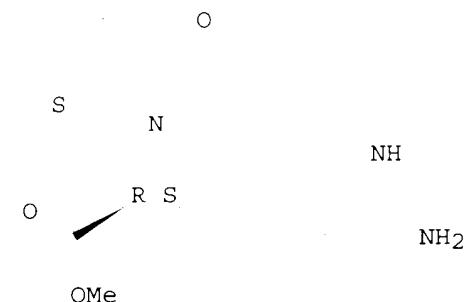
203512-10-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amidinophenyl-pyrrolidines, -pyrrolines, and -isoxazolidines as inhibitors of factor Xa)

RN 203512-01-0 CAPPLUS

CN 3-Pyrrolidinecarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-1-[2-[(2-cyanophenyl)thio]benzoyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 203512-02-1 CAPPLUS

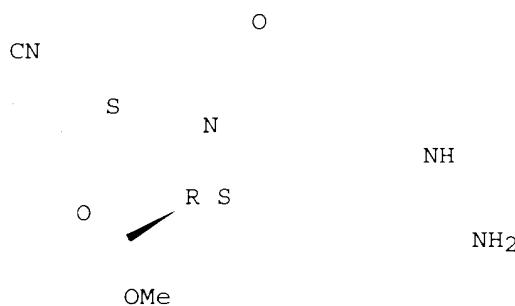
CN 3-Pyrrolidinecarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-1-[2-[(2-cyanophenyl)thio]benzoyl]-, methyl ester, trans-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 203512-01-0

CMF C27 H24 N4 O3 S

Relative stereochemistry.



CM 2

CRN 76-05-1
 CMF C2 H F3 O2

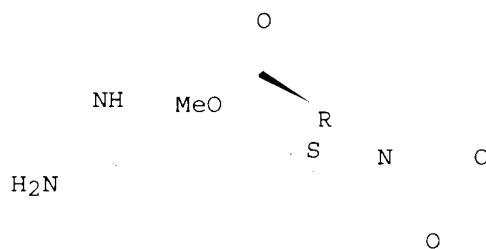
F

F C CO₂H

F

RN 203512-09-8 CAPLUS
 CN 1,3-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-,
 1-(9H-fluoren-9-ylmethyl) 3-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

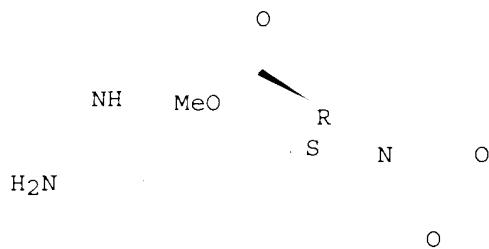


RN 203512-10-1 CAPLUS
 CN 1,3-Pyrrolidinedicarboxylic acid, 4-[3-(aminoiminomethyl)phenyl]-,
 1-(9H-fluoren-9-ylmethyl) 3-methyl ester, trans-, mono(trifluoroacetate)
 (9CI) (CA INDEX NAME)

CM 1

CRN 203512-09-8
 CMF C28 H27 N3 O4

Relative stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

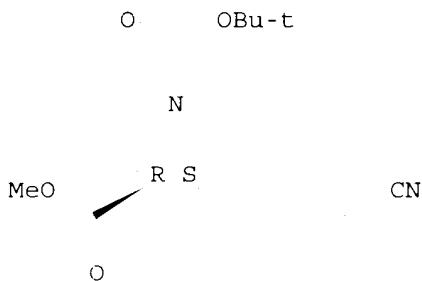
F

F C CO₂H

F

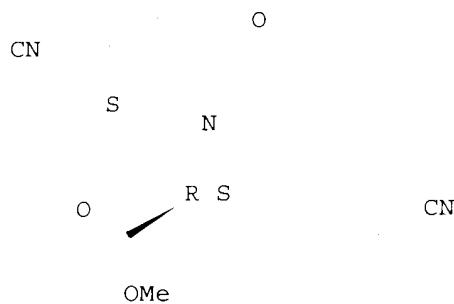
IT 203512-36-1P 203512-54-3P 203512-60-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. of amidinophenyl-pyrrolidines, -pyrrolines, and -isoxazolidines
as inhibitors of factor Xa)
RN 203512-36-1 CAPLUS
CN 1,3-Pyrrolidinedicarboxylic acid, 4-(3-cyanophenyl)-, 1-(1,1-
dimethylethyl) 3-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



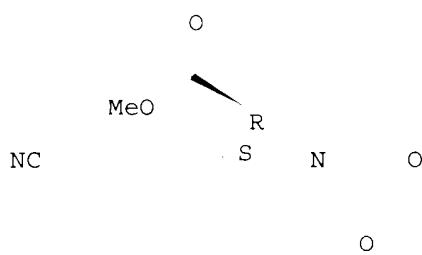
RN 203512-54-3 CAPLUS
CN 3-Pyrrolidinedicarboxylic acid, 4-(3-cyanophenyl)-1-[2-[(2-
cyanophenyl)thio]benzoyl]-, methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



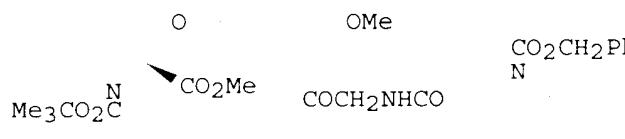
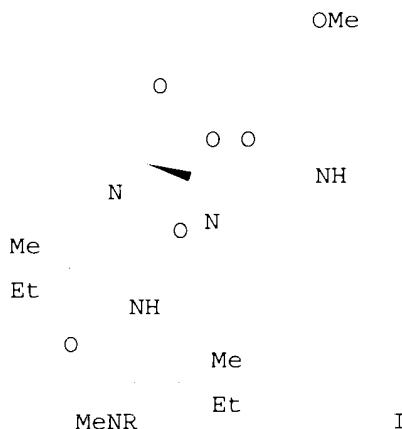
RN 203512-60-1 CAPLUS
 CN 1,3-Pyrrolidinedicarboxylic acid, 4-(3-cyanophenyl)-, 1-(9H-fluoren-9-ylmethyl) 3-methyl ester, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
 AN 1982:104572 CAPLUS
 DN 96:104572
 TI Synthesis of peptide alkaloids. Part 4. Total synthesis of zizyphines A and B
 AU Schmidt, Ulrich; Lieberknecht, Albrecht; Boekens, Hilmar; Griesser, Helmut
 CS Inst. Org. Chem., Biochem. Isotopenforsch., Univ. Stuttgart, Stuttgart,
 D-7000/80, Fed. Rep. Ger.
 SO Angewandte Chemie (1981), 93(12), 1121-2
 CODEN: ANCEAD; ISSN: 0044-8249
 DT Journal
 LA German
 GI



AB Zizyphine A (I, R = Me) and B (I, R = H) were prep'd. by a multistep procedure from 3-bromodehydroproline Me ester and 4,3-MeO(Me₃CO₂C)C₆Hg₃ONa via intermediate II.

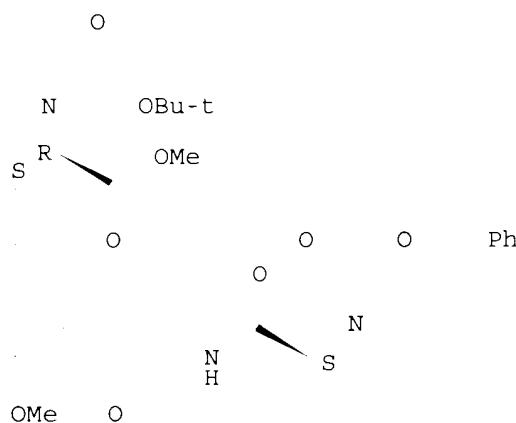
IT 79854-65-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and redn. of)

RN 79854-65-2 CAPLUS

1,2-Pyrrolidinedicarboxylic acid, 3-[4-methoxy-3-[[[[1-
[(phenylmethoxy)carbonyl]-2-pyrrolidinyl]carbonyl]amino]acetyl]phenyl]-,
1-(1,1-dimethylethyl) 2-methyl ester, [2R-[2.alpha.,3.beta. (S*)]]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.



=> d his

(FILE 'HOME' ENTERED AT 09:21:41 ON 06 MAY 2003)

FILE 'CAPLUS' ENTERED AT 09:21:57 ON 06 MAY 2003

L1 1 S 136:5917/DN
L2 ANALYZE L1 1 RN : 592 TERMS

FILE 'REGISTRY' ENTERED AT 09:22:35 ON 06 MAY 2003

L3 592 S L2
L4 415 S L3 AND (PIPERIDIN? OR PYRROLIDIN? OR AZEPIN?)
L5 2 S L4 AND PYRROLIDIN?
L6 0 S L4 AND AZEPIN?
L7 414 S L4 AND PIPERIDIN?

FILE 'CAPLUS' ENTERED AT 09:24:34 ON 06 MAY 2003

L8 941 S L7

FILE 'REGISTRY' ENTERED AT 09:24:47 ON 06 MAY 2003

L9 0 S L7 AND BAC/RL

FILE 'CAPLUS' ENTERED AT 09:26:55 ON 06 MAY 2003

L10 1 S L8 (L) BAC/RL

FILE 'REGISTRY' ENTERED AT 09:27:54 ON 06 MAY 2003

L11 0 S L7 AND THERAP?
L12 410 S L7 AND (PHENYL(L)PIPERIDIN?)

FILE 'CAPLUS' ENTERED AT 09:28:52 ON 06 MAY 2003

L13 118 S L12

FILE 'REGISTRY' ENTERED AT 09:29:15 ON 06 MAY 2003

=> s l12 and oxo?
3235711 OXO?
L14 87 L12 AND OXO?

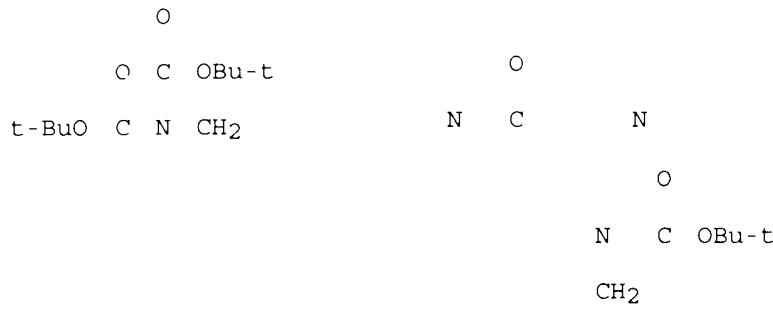
=> s l2 not l14

L16 505 L15 NOT L14

=> s l12 not l14
L17 323 L12 NOT L14

=> d scan

L17 323 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN Imidodicarbonic acid, [[3-[1-[[5-[(1,1-dimethylethoxy)carbonyl][[4-(trifluoromethoxy)phenyl]methyl]amino]-3-pyridinyl]carbonyl]-4-piperidinyl]phenyl]methyl]-, bis(1,1-dimethylethyl) ester (9CI)
MF C41 H51 F3 N4 O8



F₃C O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s l12 and (methyl(3w)amino)
 12320068 METHYL
 4140005 AMINO
 1507059 METHYL(3W)AMINO
 L18 45 L12 AND (METHYL(3W)AMINO)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	13.46	82.91
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.30

FILE 'CAPLUS' ENTERED AT 09:30:30 ON 06 MAY 2003
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FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
 FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 118
L19 1 L18

=> fil reg
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 0.42 83.33
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
ENTRY SESSION
CA SUBSCRIBER PRICE 0.00 -1.30

FILE 'REGISTRY' ENTERED AT 09:30:53 ON 06 MAY 2003
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 5 MAY 2003 HIGHEST RN 510776-00-8
DICTIONARY FILE UPDATES: 5 MAY 2003 HIGHEST RN 510776-00-8

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STNote 27, Searching Properties
in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s 117 not 118
L20 280 L17 NOT L18

=> d scan

L20 280 ANSWERS REGISTRY COPYRIGHT 2003 ACS
IN **Piperidine, 4-[3-(aminomethyl)phenyl]-1-(4-methoxybenzoyl)-, mono(trifluoroacetate) (9CI)**
MF C20 H24 N2 O2 . C2 H F3 O2

CM 1

O OMe

N C

H₂N CH₂

CM 2

F

F C CO₂H

F

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> s 120 and aminomethyl
48240 AMINOMETHYL
L21 259 L20 AND AMINOMETHYL

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.62	87.95
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-1.30

FILE 'CAPLUS' ENTERED AT 09:31:35 ON 06 MAY 2003
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FILE COVERS 1907 - 6 May 2003 VOL 138 ISS 19
FILE LAST UPDATED: 5 May 2003 (20030505/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 121
L22 1 L21

=> d bib abs

L22 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1296972	A1	20030402	EP 2001-930925	20010427
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001011206	A	20030415	BR 2001-11206	20010427
	NO 2002005601	A	20030106	NO 2002-5601	20021121
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
	WO 2001-US13811	W	20010427		
OS	MARPAT	136:5917			
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prep'd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NEt, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 375847-91-9P 375847-93-1P
RL: BSU (Biological study, unclassified); BYP (Byproduct); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (drug; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors)

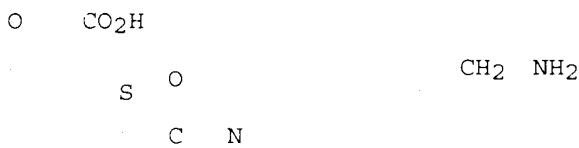
RN 375847-91-9 CAPLUS

CN Benzo[c]thiophene-1-carboxylic acid, 3-[(4-[3-(aminomethyl)phenyl]-1-piperidinyl)carbonyl]-4,5,6,7-tetrahydro-5,5-dimethyl-7-oxo-,
mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 375847-90-8

CMF C24 H28 N2 O4 S



Me

CM 3

CBN 76-05-1

CRN 78-05-1
CME C2 H E3 03

F

$$\text{F} \quad \text{C} \quad \text{CO}_2\text{H}$$

F

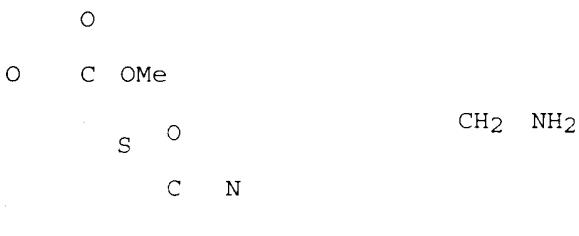
RN 375847-93-1 CAPLUS

CN Benzo[c]thiophene-1-carboxylic acid, 3-[[4-[3-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-4,5,6,7-tetrahydro-5,5-dimethyl-7-oxo-, methyl ester, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 375847-92-0

CMF C25 H30 N2 O4 S



CM 2

CRN 76-05-1
CMF C2 H F3 O2

F

F C CO₂H

F

IT 375846-93-8P 375846-94-9P 375846-95-0P
375846-96-1P 375846-97-2P 375846-98-3P
375846-99-4P 375847-00-0P 375847-01-1P
375847-02-2P 375847-03-3P 375847-04-4P
375847-05-5P 375847-06-6P 375847-07-7P
375847-08-8P 375847-09-9P 375847-10-2P
375847-11-3P 375847-12-4P 375847-13-5P
375847-15-7P 375847-17-9P 375847-19-1P
375847-21-5P 375847-23-7P 375847-25-9P
375847-27-1P 375847-29-3P 375847-31-7P
375847-33-9P 375847-34-0P 375847-35-1P
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375847-44-2P 375847-46-4P 375847-48-6P
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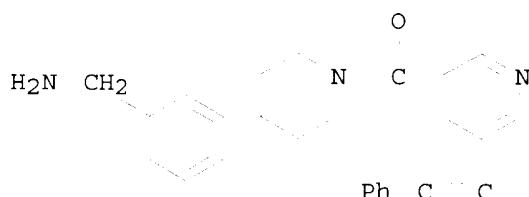
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375851-17-5P 375851-19-7P 375851-21-1P
375851-23-3P 375851-25-5P 375851-27-7P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
study); PREP (Preparation); USES (Uses)

(drug; prepn. of (hetero)arylacyl-piperidinyl-benzylamines for use as
tryptase inhibitors)

RN 375846-93-8 CAPLUS

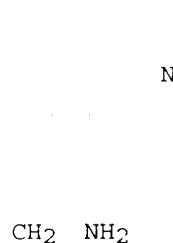
CN Piperidine, 4- [3- (aminomethyl)phenyl]-1- [[5- (phenylethynyl)-3-
pyridinyl]carbonyl] -, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

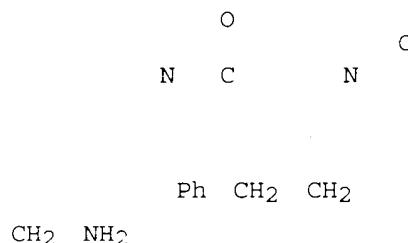
RN 375846-94-9 CAPLUS

CN Piperidine, 4- [3- (aminomethyl)phenyl]-1- [[5- (2-phenylethyl)-3-
pyridinyl]carbonyl] -, dihydrochloride (9CI) (CA INDEX NAME)



●₂ HCl

RN 375846-95-0 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[[1-oxido-5-(2-phenylethyl)-3-pyridinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)



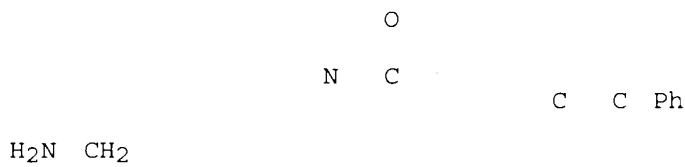
• HCl

RN 375846-96-1 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-(3-quinolinylcarbonyl)-, dihydrochloride (9CI) (CA INDEX NAME)



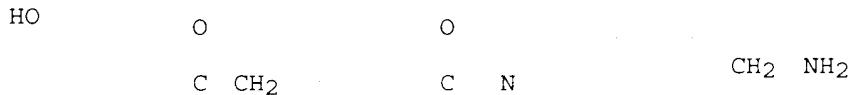
● 2 HCl

RN 375846-97-2 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[3-(phenylethynyl)benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 375846-98-3 CAPLUS
CN Piperidine, 4-[3-(aminomethyl)phenyl]-1-[3-[2-(4-hydroxyphenyl)-2-oxoethyl]benzoyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

=> s (aminomethyl(1)amidin?) and (coagul? or anticoagul?)
18988 AMINOMETHYL
14007 AMIDIN?
88 AMINOMETHYL(L)AMIDIN?
122960 COAGUL?
25286 ANTICOAGUL?
L1 27 (AMINOMETHYL(L)AMIDIN?) AND (COAGUL? OR ANTICOAGUL?)

=> s 11 and py<2000
19718935 PY<2000
L2 16 L1 AND PY<2000

=> s 12 and us/pc
1152526 US/PC
L3 11 L2 AND US/PC

=> d bib abs 1-11

L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 2002:354079 CAPLUS
DN 136:355487
TI Preparation of meta-benzamidine derivatives of amino acids or dipeptides as serine protease inhibitors
IN Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John
PA UK
SO U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S. Ser. No. 485,678.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 13

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002055522	A1	20020509	US 2001-988082	20011119 <--
	WO 9911658	A1	19990311	WO 1998-GB2605	19980828 <--
		W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
		RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	WO 2000077027	A2	20001221	WO 2000-GB2291	20000613
	WO 2000077027	A3	20010525		
		W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
		RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
PRAI	GB 1997-18392	A	19970829		
	GB 1998-3173	A	19980213		
	WO 1998-GB2605	W	19980828		
	GB 1999-13823	A	19990614		
	US 1999-142064P	P	19990702		

US 2000-485678 A2 20000225
 WO 2000-GB2291 A2 20000613
 GB 1999-18741 A 19990809
 GB 1999-29552 A 19991214
 GB 1999-29553 A 19991214
 OS MARPAT 136:355487
 GI

Cy

X X Y L Lp(D)n

R3

R¹R²N NR¹ I

AB Title compds. I [R₁, R₂ = H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl; R₃ = R₁, R₂, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulfonyl, alkylsulfenyl, alkylsulfonamido, alkylaminosulfonyl, haloalkoxy, haloalkyl; X = C, N, O, S, CO, CR₁, C(R₁)₂, NR₁ with at least one X being C, CO, CR₁ or C(R₁)₂, with the proviso that if the benzamidine group is unsubstituted and the X-X group is -CH₂C(R₁)₂- , then R₁ = H or attached to the alkylene carbon atom by a heteroatom; L = org. linker contg. 1-5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y = N, CR₁; YL = cyclic group optionally substituted by groups R₃ or Ph optionally substituted by R₃; Lp = lipophilic alkyl, heterocyclic, alkenyl, alkaryl, (poly)cycloalkyl, cycloalkenyl, aryl, aralkyl, haloalkyl, or a combination of two or more such groups optionally substituted by oxa, oxo, aza, thio, halo, amino, hydroxy or by R₃; D = H bond donor group; n = 0-2], or corresponding compds. in which the (un)substituted **amidino** group R₁R₂NC(:NR₁) is replaced with an (un)substituted **aminomethyl** group, or their physiol. tolerable salts were prep'd. as serine protease inhibitors useful as antithrombotic agents. 3-**Amidino**- and 3-(**aminomethyl**)benzoyl-D-phenylglycine 4-aminomethylcyclohexylmethylamide are among 190 compds. synthesized.

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 1999:69898 CAPLUS

DN 130:125409

TI Preparation of peptides as **anticoagulant** agents

IN Klimkowski, Valentine Joseph; Schacht, Aaron Leigh; Wiley, Michael Robert

PA Eli Lilly and Company, USA

SO U.S., 20 pp.

CODEN: USXXAM

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5863929	A	19990126	US 1997-879637	19970620 <--
	US 6008367	A	19991228	US 1999-237012	19990125 <--
	US 6034104	A	20000307	US 1999-237010	19990125 <--
	US 6160176	A	20001212	US 1999-237011	19990125 <--
	US 6552038	B1	20030422	US 2000-614179	20000711 <--
PRAI	US 1996-20371P	P	19960625		

OS US 1997-879637 A3 19970620
 OS US 1999-237011 A3 19990125
 OS MARPAT 130:125409
 AB Peptides XCO-Y-G-R [X = 3,4-dihydroisoquinolin-1-yl or -3-yl optionally alkylated at 1, 2, and/or 3-position or corresponding hexahydro derivs. or cyclopentano- or cycloheptano analogs; Y = NRgCH2 (Rg = alkyl, cycloalkyl, (CH2)p-L-(CH2)q-T', where L is a bond, O, S, or NH; T' is alkyl, cycloalkyl, CO2H, CONH2, or aryl group; p = 0-4; q = 0-3), 1,2-azetidinediyl, 1,2-pyrrolidinediyl or derivs., 1,2-piperidinediyl; G = CONHCH2S, CH2NH(CH2)s (s = 1, 2), CH2NHCO, (CH2)tO (t = 1, 2, 3); R = 4-amidino-3-hydroxyphenyl group bearing 0-3 fluoro substituents] were prepd. as **anticoagulants**. Thus, N-[(4-(aminoiminomethyl)-3-hydroxyphenyl)methyl]-1-[(1R,4aR,8aR)-perhydroisoquinolin-1-ylcarbonyl]-L-prolinamide dihydrochloride was prepd. via amidation of a proline deriv. with 4-**aminomethyl**-2-hydroxybenzamide dihydrochloride.

RE.CNT 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2003 ACS
 AN 1999:35065 CAPLUS
 DN 130:110166
 TI Preparation of amidinophenylpropionyltetrahydroquinolines and related compounds as antithrombotics.
 IN Heckel, Armin; Soyka, Rainer; Grell, Wolfgang; Haaksma, Eric; Binder, Klaus; Zimmermann, Rainer
 PA Boehringer Ingelheim Pharma K.-G., Germany
 SO Ger. Offen., 50 pp.
 CODEN: GWXXBX
 DT Patent
 LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19727117	A1	19990107	DE 1997-19727117	19970626 <--
	WO 9900371	A1	19990107	WO 1998-EP3800	19980622 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9887279	A1	19990119	AU 1998-87279	19980622 <--
	EP 991624	A1	20000412	EP 1998-938621	19980622
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002511088	T2	20020409	JP 1999-505265	19980622
	MX 9911261	A	20000630	MX 1999-11261	19991206
	US 6300342	B1	20011009	US 1999-457961	19991209 <--
PRAI	DE 1997-19727117	A	19970626		
	WO 1998-EP3800	W	19980622		

OS MARPAT 130:110166

GI

R?	A	R?
	N	W R?
YB		
	R?	I

AB Title compds. [I; Ra = H, NO₂, amino, aminocarbonyl; Rb = cyano, **aminomethyl**, (substituted) **amidino**; Rc, Rd = H, F, Cl, Br, iodo, Me, MeO, NO₂, amino; A = (substituted) ethylene, ethylenylene, propylene, etc.; B = bond, (substituted) methylene, ethylene, ethenylene, propylene, etc.; W = N, CH; Y = CH₂, CO, CS], were prepd. Thus, 1-[3-(4-**amidinophenyl**)propionyl]-1,2,3,4-tetrahydroquinoline-6-carboxylic acid methyl-N-phenylamide (prepn. given) had a thrombin time ED₂₀₀ = 0.02 .mu.M.

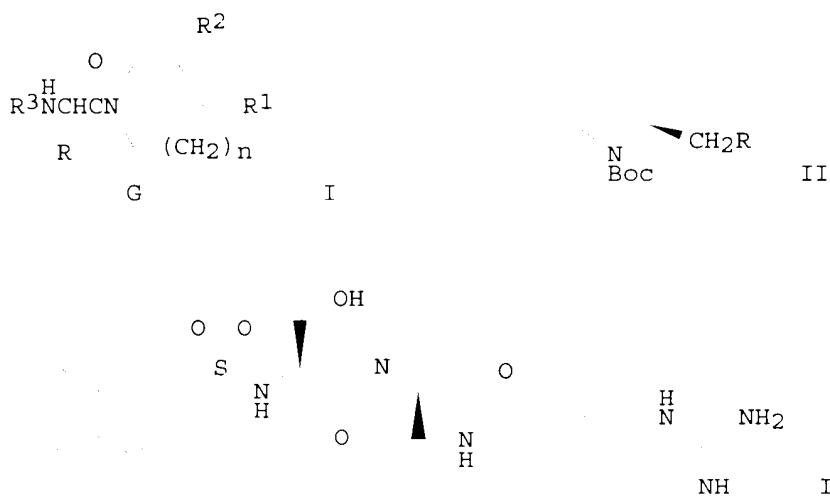
L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2003 ACS
 AN 1998:604913 CAPLUS
 DN 129:216617
 TI Preparation of amidinophenylethylbenzimidazolylcarboxamides and related compounds as thrombin inhibitors.
 IN Hauel, Norbert; Ries, Uwe; Priepeke, Henning; Wienen, Wolfgang; Stassen, Jean Marie
 PA Boehringer Ingelheim Pharma K.-G., Germany
 SO PCT Int. Appl., 201 pp.
 CODEN: PIXXD2
 DT Patent
 LA German
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9837075	A1	19980827	WO 1998-EP865	19980216 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	DE 19706229	A1	19980820	DE 1997-19706229	19970218 <--
	DE 19751939	A1	19990722	DE 1997-19751939	19971124 <--
	AU 9863991	A1	19980909	AU 1998-63991	19980216 <--
	AU 742593	B2	20020110		
	EP 966454	A1	19991229	EP 1998-909468	19980216 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	EE 9900359	A	20000215	EE 1999-359	19980216
	NZ 337323	A	20001124	NZ 1998-337323	19980216
	JP 2001509815	T2	20010724	JP 1998-536234	19980216
	JP 3343359	B2	20021111		
	NO 9903945	A	19991015	NO 1999-3945	19990817 <--
	US 6414008	B1	20020702	US 2000-688260	20001013 <--
PRAI	DE 1997-19706229	A	19970218		
	DE 1997-19751939	A	19971124		
	US 1997-44421P	P	19970429		
	WO 1998-EP865	W	19980216		
	US 1998-25690	A3	19980218		
	US 2000-544931	A1	20000406		
OS	MARPAT	129:216617			
AB	Ra-A-Het-B-Ar-E	[A = CO, SO ₂ ; B = CH ₂ CH ₂ , OCH ₂ , SCH ₂ , SOCH ₂ , SO ₂ CH ₂ , NR ₁ CH ₂ ; R ₁ = H, alkyl; E = cyano, RbNHC(:NH); Rb = H, OH, alkyl, group cleavable in vivo; Ar = (substituted) phenylene, naphthylene, thiophenylene, thiazolylene, pyridinylene, pyrimidinylene, pyrazinylene, pyridazinylene; Het = specified bicyclic heterocycl; Ra = (substituted) alkyl, amino] were prepd. Thus, 1-methyl-2-[N-(4- amidinophenyl) aminomethyl]benzimidazol-5-ylcarboxylic acid N-(2-pyridyl)-N-(2-carboxyethyl)amide (prepn. given) gave a thrombin time ED ₂₀₀ of 0.03 .mu.M.			

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2003 ACS
AN 1997:26985 CAPLUS
DN 126:104429
TI Preparation of heterocyclic peptide thrombin inhibitors
IN Kimball, Spencer D.; Das, Jagabandhu; Lau, Wan F.; Hall, Steven E.; Han, Wen Ching
PA Bristol-Myers Squibb Company, USA
SO U.S., 95 pp., Cont.-in-part of U.S. Ser. No. 146,714, abandoned.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 6

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5583146	A	19961210	US 1995-373334	19950117 <--
	US 6534536	B1	20030318	US 1994-213964	19940316 <--
	CN 1109468	A	19951004	CN 1994-103732	19940331 <--
	US 5741792	A	19980421	US 1995-555560	19951108 <--
	US 5741799	A	19980421	US 1995-555561	19951108 <--
PRAI	US 1992-984640	B2	19921202		
	US 1993-56017	B2	19930503		
	US 1993-56279	B2	19930503		
	US 1993-112153	B2	19930826		
	US 1993-112155	B2	19930826		
	US 1993-146714	B2	19931110		
	US 1994-207725	B2	19940314		
	US 1994-207726	B2	19940314		
	US 1994-213964	A2	19940316		
	US 1995-373334	A3	19950117		
OS	MARPAT	126:104429			
GI					



AB Heterocyclic thrombin inhibitors are provided which have the structure I
[G = CONH(CH₂)_p-Q-A-R₄, CH₂-X_a-A₁-R_{3a}; R = H, hydroxyalkyl, aminoalkyl, amidoalkyl, alkyl, cycloalkyl, aryl, arylalkyl, alkenyl, alkynyl, arylalkoxyalkyl, (un)protected amino acid side chain; R₁, R₂ = independently H, lower alkyl, cycloalkyl, aryl, OH, alkoxy, thioalkyl,

thioaryl, amino, alkylamino; R1R2 = O, S; CR1CR2 = cycloalkyl, aryl, heteroaryl ring; R3 = H, SO2R6, COR7; R3a = guanidine, **amidine**, amino; R4 = guanidine, **amidine**, **aminomethyl**; R6 = lower alkyl, aryl, arylalkyl, heteroaryl, quinolinyl, tetrahydroquinolinyl; R7 = lower alkyl, aryl, cycloheteroalkyl, heteroaryl; n = 0-2; p = 0-5; Q = single bond, CO; A = NH, S, 4-8 membered aryl, cycloalkyl, azacycloalkyl, aza heterocycloalkyl ring, Q1; A1 = bond, C2-6 alkyl, alkenyl, alkynyl; X = CH2, O, S, NH; Xa = NH, S, S(O), SO2, O; q = 0-4; Y1, Y2 = independently H, lower alkyl, halo, including all stereoisomers and pharmaceutically acceptable salts thereof, are thus useful in inhibiting formation of thrombi (no data). Thus, substitution of protected prolinol deriv. II (Boc = Me3CO2C; R = O3SC6H4Me-4) with NaN3 gave the corresponding azide II (R = N3), which underwent catalytic hydrogenation to give amine II (R = NH2). Coupling of II (R = NH2) with HO2C(CH2)3NHZ (Z = CO2CH2Ph) gave amide II [R = NHCO(CH2)3NHZ], which was deprotected with HCl, coupled with Boc-Ser(CH2Ph)-OH, deprotected, sulfonylated with 2-naphthylsulfonyl chloride, deprotected, and guanylated with **amidinesulfonic** acid to give target compd. III.

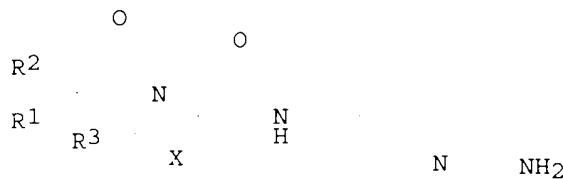
L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2003 ACS
 AN 1996:738089 CAPLUS
 DN 126:18793
 TI [(Aminoiminomethyl)piperidinyl]methyl]proline amides and related compounds useful as thrombin inhibitors
 IN Vacca, Joseph P.; Lumma, William C.; Brady, Stephen F.; Tucker, Thomas Joseph
 PA Merck and Co., Inc., USA
 SO PCT Int. Appl., 48 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9632110	A1	19961017	WO 1996-US4679	19960404 <--
	W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5629324	A	19970513	US 1995-419683	19950410 <--
	CA 2217682	AA	19961017	CA 1996-2217682	19960404 <--
	AU 9655348	A1	19961030	AU 1996-55348	19960404 <--
	AU 698705	B2	19981105		
	EP 820287	A1	19980128	EP 1996-912574	19960404 <--
	EP 820287	B1	20020327		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
	JP 11503455	T2	19990326	JP 1996-531066	19960404 <--
	AT 214928	E	20020415	AT 1996-912574	19960404
	ES 2172657	T3	20021001	ES 1996-912574	19960404
PRAI	US 1995-419683	A2	19950410		
	WO 1996-US4679	W	19960404		
OS	MARPAT	126:18793			
GI					

Z

Q=

OH



NH I

NH



II

AB Title compds. I and their pharmaceutically acceptable salts are disclosed [wherein R1, R2 = H, (un)substituted Ph, alkyl, cycloalkyl, etc.; R1R2 may form 4- to 7-membered carbocycle with 1-2 optional N,O, or S atoms; R3 = H, HO(CH₂)₀₋₄; or CR1R2R3 = tricyclic group Q (where Z = CH, O, or bond); X = (CH₂)₁₋₂, NR₁CH₂, SCH₂]. These compds. inhibit thrombin and assocd. thrombosis. For example, L-proline Me ester HCl underwent a sequence of N-acylation with Ph₂CHCH₂CO₂H (83%), alk. sapon. of the ester (94%), amidation with 1-(tert-butoxycarbonyl)-4-(aminomethyl)piperidine using EDC and HOBr (79%), acidic removal of the BOC group (100%), and guanylation of the piperidine N with **amidinesulfonic acid**, to give title compd. II [G = Ph₂CHCH₂]. In a test for inhibition of thrombin, the above compd. had Ki of 2.7 nM, and the similarly prep'd. compd. II [G = 9-hydroxy-9-fluorenyl] had Ki of 1.1 nM.

L3 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 1996:623129 CAPLUS

DN 125:276585

TI Preparation of dipeptide amidinobenzylamides and related compounds as thrombin inhibitors.

IN Seitz, Werner; Mack, Helmut; Zierke, Thomas; Boehm, Hans-Joachim; Hoeffken, Hans Wolfgang; Koser, Stefan; Pfeiffer, Thomas; Hornberger, Wilfried

PA BASF A.-G., Germany

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9624609	A1	19960815	WO 1996-EP472	19960206 <--
	W: AU, BG, BR, CA, CN, CZ, FI, HU, JP, KR, MX, NO, NZ, PL, SG, SK, TR, UA, US, AZ, BY, KG, KZ, RU, TJ, TM				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	DE 19504504	A1	19960814	DE 1995-19504504	19950210 <--

DE 19506610	A1	19960829	DE 1995-19506610	19950224	<--
AU 9647875	A1	19960827	AU 1996-47875	19960206	<--
AU 706834	B2	19990624			
EP 809651	A1	19971203	EP 1996-903987	19960206	<--
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE					
BR 9607412	A	19980707	BR 1996-7412	19960206	<--
JP 10513462	T2	19981222	JP 1996-523967	19960206	<--
US 5932567	A	19990803	US 1997-875515	19970730	<--
FI 9703282	A	19970808	FI 1997-3282	19970808	<--
NO 9703657	A	19971003	NO 1997-3657	19970808	<--
PRAI DE 1995-19504504		19950210			
DE 1995-19506610		19950224			
WO 1996-EP472		19960206			
OS MARPAT 125:276585					
GI					

N $(\text{CH}_2)_m$
 $Q^1 =$

CO

AB R1SO2ABNHDC(:NH)NH2 [R1 = OH, alkyl, fluoroalkyl, cycloalkyl, aralkyl, aryl, heteroaryl, etc.; A = NHCR4R5CO; R4 = H, alkyl, cycloalkyl, aryl, aralkyl; R5 = H, alkyl, cycloalkyl, cycloalkylmethyl, bicycloalkyl(methyl), adamantyl(methyl), etc.; B = (substituted) Q1; m = 2-4; D = (substituted) PhCH2, heteroaryl methyl], were prepd. as thrombin inhibitors (no data). Thus, BOC-Pro-OH was coupled with 4-aminomethyl-3-methoxybenzonitrile (prepn. given) using hydroxysuccinimide/DCC in CH2C12 to give 65% BOC-Proline (4-cyano-2-methoxy)benzylamide. The latter was deprotected and coupled with BOC-D-Phe(4-OMe)-OH using diisopropylethylamine/propanephosphonic anhydride to give BOC-D-(4-methoxyphenylalanyl)proline (4-cyano-2-methoxy)benzylamide. The latter was elaborated in several steps to title compd. N-methylsulfonyl-D-(4-methoxy)phenylalanylproline (2-methoxy-4-amidino)benzylamide acetate salt.

L3 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2003 ACS
 AN 1996:397160 CAPLUS
 DN 125:58341
 TI Preparation of naphthalene-, isoquinoline- and chroman-acetic acid derivatives as platelet aggregation inhibitors
 IN Okumura, Kunio; Yokoyama, Isao; Shimazaki, Toshiyuki; Miyamoto, Michihiko; Yamashita, Hiroyuki; Kibayashi, Kenji; Yutaka, Takanori; Yazawa, Kouhei
 PA Mitsui Toatsu Chemicals, Inc., Japan
 SO Eur. Pat. Appl., 30 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	EP 709370	A1	19960501	EP 1995-116893	19951026 <--
	EP 709370	B1	19990113		
R: DE, FR, GB, IT					
	US 5629321	A	19970513	US 1995-544583	19951018 <--
	JP 08231486	A2	19960910	JP 1995-275433	19951024 <--
	JP 2951875	B2	19990920		
PRAI	JP 1994-264188		19941027		
OS	MARPAT 125:58341				

GI

COOZ

B W X

A Y I

NC

COOMe

O

II

AB The title compds. [I; A = **amidino**, guanidino, **aminomethyl**; B = CH₂O, OCH₂, CH₂N(R₁), N(R₁)CH₂, CON(R₁), N(R₁)CO (wherein R₁ = H, C₁-4 alkyl); W-X = CH₂CH, CH₂N; CH:C; Y = CH₂, O; Z = H, C₁-4 alkyl], useful for prevention and therapy of thrombosis and restenosis or reocclusion after percutaneous transluminal coronary angioplasty or percutaneous transluminal coronary recanalization, were prep'd. and formulated. Reaction of Me 7-hydroxy-1,2,3,4-tetrahydronaphthalene-2-acetate with 4-NCC₆H₄CH₂Br in the presence of K₂CO₃ in MeCOEt followed by treatment of the intermediate II with gaseous HCl in MeOH and then addn. AcONH₄ afforded I.HCl [A = **amidino**; B = CH₂O; W-X = CH₂CH; Y = CH₂; Z = Me] which showed IC₅₀ of 22 .mu.M against platelet aggregation in Guinea pig.

L3 ANSWER 9 OF 11 CAPLUS COPYRIGHT 2003 ACS

AN 1995:777645 CAPLUS

DN 123:169604

TI Oxazolidinone derivatives as adhesion-receptor antagonists.

IN Raddatz, Peter; Gante, Joachim; Juraszky, Horst; Wurziger, Hanns; Pruecher, Helmut; Bernotat-Danielowski, Sabine; Melzer, Guido

PA Merck Patent G.m.b.H., Germany

SO Eur. Pat. Appl., 18 pp.

CODEN: EPXXDW

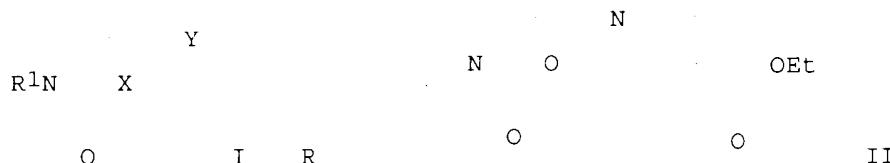
DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 623615	A1	19941109	EP 1994-106049	19940419 <--
	EP 623615	B1	19990630		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	DE 4405633	A1	19941103	DE 1994-4405633	19940222 <--
	AT 181735	E	19990715	AT 1994-106049	19940419 <--
	ES 2134870	T3	19991016	ES 1994-106049	19940419 <--
	AU 9460643	A1	19941103	AU 1994-60643	19940421 <--
	AU 675698	B2	19970213		
	SK 281469	B6	20010409	SK 1994-484	19940426
	CN 1097421	A	19950118	CN 1994-105008	19940427 <--
	CN 1052231	B	20000510		
	CZ 285761	B6	19991117	CZ 1994-1019	19940427 <--
	JP 07002847	A2	19950106	JP 1994-92058	19940428 <--

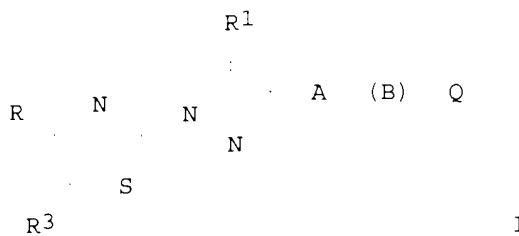
PL 178131	B1	20000331	PL 1994-303242	19940428
CA 2122571	AA	19941102	CA 1994-2122571	19940429 <--
NO 9401592	A	19941102	NO 1994-1592	19940429 <--
ZA 9402973	A	19950118	ZA 1994-2973	19940429 <--
US 5532255	A	19960702	US 1994-234691	19940429 <--
RU 2145961	C1	20000227	RU 1994-15184	19940429
HU 70541	A2	19951030	HU 1994-1274	19940502 <--
PRAI DE 1993-4314378	A	19930501		
DE 1994-4405633	A	19940222		
OS MARPAT 123:169604				
GI				



AB Title compds. I [X = O, S, NH, NA; Y = R2-bearing aziridino, azetidino, pyrrolidino, piperidino, etc., 4-(R4)-bearing piperazino, optionally substituted by OZ, SZ, NZ2, and/or carbonyloxy; Z = H, A, C1-11 acyl, Ph(CkH2k); R1 = Ph substituted by cyano, **aminomethyl**, **amidino**, guanidino, and certain other N-contg. functional groups; R2 = (CmH2m)CO2R3, (CnH2n)O(CpH2p)CO2R3; R3 = H, A, CH2Ph; R4 = H, A, CH2Ph, (CmH2m)CO2R3; A = C1-6 alkyl; k, m = 0-3; n = 0-2; p = 1-3] and salts are claimed. I are claimed useful for therapy of thrombosis, heart infarct, apoplexy, osteoporosis, inflammation, tumors, etc., and also have antimicrobial activity (no data). For example, reaction of 3-(4-cyanophenyl)-5-(methanesulfonyloxyethyl)-2-oxazolidinone [prepn. given] with 4-piperidinecarboxylic acid Et ester in MeCN in the presence of K2CO3 and KI under heating gave title compd. II (R = cyano). Sequential reaction of the latter with H2S and Et3N in pyridine, MeI in acetone, and NH4OAc in MeOH, gave II (R = **amidino**). Sapon. of this ester gave the corresponding acid, which is specifically claimed.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2003 ACS
 AN 1995:264625 CAPLUS
 DN 122:56039
 TI Substituted thiazole derivatives useful as platelet aggregation inhibitors
 IN Sanfilippo, Pauline J.; Urbanski, Maud; Carson, John R.; Carmosin, Richard J.
 PA McNeil-PPC, Inc., USA
 SO U.S., 22 pp.
 CODEN: USXXAM
 DT Patent
 LA English
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 5342851	A	19940830	US 1992-958193	19921007 <--
PRAI US 1992-958193		19921007		
OS MARPAT 122:56039				
GI				



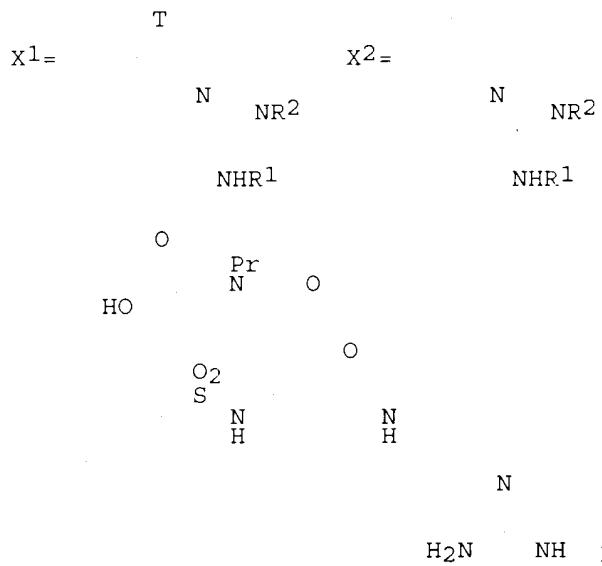
AB This invention relates to substituted thiazole derivs. I [R and R3 are the same or different and are selected from H, OH, CO2H, C1-4-alkylcarboxy, C1-8-alkyl, CF3, halo, (un)substituted Ph, etc.; R1 is selected from H, halo, OH, CO2H, C1-4-alkylcarboxy, C1-5-alkyl, CF3, (un)substituted Ph; R2 = H, C1-5-alkyl; A is selected from carbonyl, carboxyl, carboxamido, amido, oxymethyl, **aminomethyl**, methylene; B is selected from C1-9-alkyl, C1-9 branched alkyl, Ph, C1-5-aralkyl; Q is selected from OH, C1-5-alkoxy, halo, cyano, CO2H, C1-5-alkoxycarbonyl, NR4R5, where R4 and R5 are independently H, C1-5-alkyl, C3-8-cycloalkyl, or NR4R5 = heterocycle or guanidine, urea, thiourea, hydrazine, (un)substituted **amidine**]. These compds. are useful as inhibitors of platelet aggregation and inhibitors of adhesion mols. and may be provided in pharmaceutical compns. and in methods of treating reperfusion thrombosis injury in patients. IC₅₀ values (the concn. of the compd. in .mu.M at which the increase in light transmission = x% in drug-treated platelet conc. vs. control) were as high as x = 90 at 20 .mu.M. Formulations were given.

L3 ANSWER 11 OF 11 CAPLUS COPYRIGHT 2003 ACS
 AN 1994:483062 CAPLUS
 DN 121:83062
 TI N-Amidinopiperidinyl-(3/4)- or N-amidino-1,4-oxazinyl-(2)-substituted sulfonamides, process for their preparation, and use as thrombin inhibitors
 IN Ackermann, Jean; Banner, David; Gubernator, Klaus; Hilpert, Kurt; Schmid, Gerard
 PA Hoffmann-La Roche, F., und Co. A.-G., Switz.
 SO Eur. Pat. Appl., 43 pp.
 CODEN: EPXXDW
 DT Patent
 LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 559046	A1	19930908	EP 1993-102767	19930222 <--
	EP 559046	B1	20010711		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2089972	AA	19930907	CA 1993-2089972	19930219 <--
	AT 203013	E	20010715	AT 1993-102767	19930222
	ES 2161217	T3	20011201	ES 1993-102767	19930222
	US 5405854	A	19950411	US 1993-21919	19930224 <--
	ZA 9301403	A	19930906	ZA 1993-1403	19930226 <--
	AU 9333916	A1	19930909	AU 1993-33916	19930301 <--
	AU 665230	B2	19951221		
	IL 120727	A1	19980816	IL 1993-120727	19930301 <--
	HU 70156	A2	19950928	HU 1993-572	19930302 <--
	RO 112863	B3	19980130	RO 1993-294	19930303 <--
	BR 9300753	A	19930908	BR 1993-753	19930304 <--
	RU 2133739	C1	19990727	RU 1993-4666	19930304 <--
	NO 9300819	A	19930907	NO 1993-819	19930305 <--
	CN 1076690	A	19930929	CN 1993-101908	19930305 <--
	JP 06025195	A2	19940201	JP 1993-69080	19930305 <--

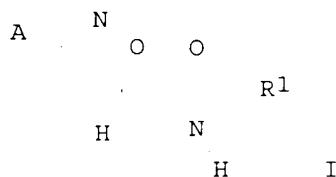
JP 07080848	B4	19950830		
PL 173030	B1	19980130	PL 1993-297960	19930305 <--
CZ 286926	B6	20000816	CZ 1993-346	19930305
US 5578594	A	19961126	US 1994-361274	19941221 <--
US 5677448	A	19971014	US 1996-689743	19960813 <--
US 5763604	A	19980609	US 1997-869558	19970604 <--
FI 9901361	A	19990614	FI 1999-1361	19990614 <--
PRAI CH 1992-728	A	19920306		
CH 1993-180	A	19930121		
US 1993-21919	A3	19930224		
IL 1993-104893	A3	19930301		
FI 1993-990	A3	19930305		
US 1994-361274	A3	19941221		
US 1996-689743	A3	19960813		
OS MARPAT 121:83062				
GI				



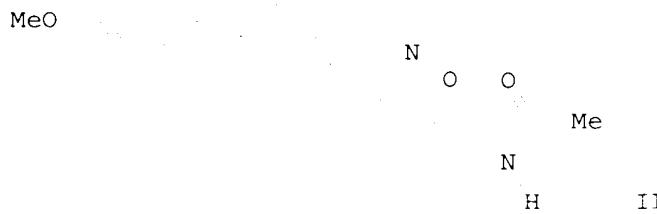
AB Title compds. ASO2N(Y)MCON(Q)CH₂X [I; X = oxazinyl and piperidinyl groups X₁ or X₂; T = CH₂ or O; R₁, R₂ = H, alkoxy carbonyl; Y = H and in some cases CH₂CO₂H or SO₂A'; A, A' = (hetero)aryl, (cyclo)alkyl, heterocyclyl; Q = H, certain (un)substituted alkyl; M = CH(Z), CH(Z)CH₂; Z = various pendant groups, mostly contg. amide functions] were prep'd. as drugs, primarily as inhibitors of thrombin-induced platelet aggregation and fibrinogen **coagulation**. For example, condensation of (S)-1-**amidino-3-(aminomethyl)piperidine-2HCl** with the corresponding acid by the BOP method gave (S)-[N-allyl-3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-(2-naphthylsulfonylamino)propionyl]amino]acetic acid Et ester hydrochloride, which underwent hydrolysis by aq. NaOH and hydrogenation over Pd/C to give title compd. (S)-[[3-[(S)-1-(aminoiminomethyl)piperidin-3-ylmethylcarbamoyl]-2-(2-naphthylsulfonylamino)propionyl]propylamino]acetic acid (II). I showed high specificity for inhibition of thrombin over other serine proteases, with II having $K_i = 0.22$ and 4300 nM for thrombin and trypsin, resp. (ratio = 19,545). Approx. 200 I were prep'd. in 73 synthetic examples.

AN 1998:147317 CAPLUS
 DN 128:192646
 TI Preparation of isoxazolines as antimicrobials
 IN Barbachyn, Michael R.; Thomas, Richard C.; Cleek, Gary J.
 PA Pharmacia & Upjohn Company, USA; Barbachyn, Michael R.; Thomas, Richard
 C.; Cleek, Gary J.
 SO PCT Int. Appl., 103 pp.
 CODEN: PIKXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9807708	A1	19980226	WO 1997-US13934	19970815
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739736	A1	19980306	AU 1997-39736	19970815
	EP 920421	A1	19990609	EP 1997-937156	19970815
	EP 920421	B1	20021106		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 5990136	A	19991123	US 1997-999753	19970815
	JP 2000516245	T2	20001205	JP 1998-510781	19970815
	AT 227277	E	20021115	AT 1997-937156	19970815
	US 6093736	A	20000725	US 1999-386647	19990831
PRAI	US 1996-24287P	P	19960821		
	US 1997-999753	A3	19970815		
	WO 1997-US13934	W	19970815		
OS	MARPAT	128:192646			
GI					



O



AB The title compds. [I; R1 = H, (un)substituted C1-8 alkyl, C3-6 cycloalkyl,

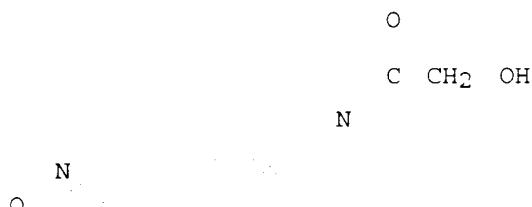
etc.; A = substituted Ph, 5-6 membered heteroaryl, .beta.-carbolinyl, etc.], useful as antimicrobial agents, were prepd. Thus, cyclization of 4-bromo-N-hydroxybenzenecarboximidoyl chloride with allyl alc. followed by methanesulfonylation of the resulting 4,5-dihydro-3-(4-bromophenyl)-5-(hydroxymethyl)isoxazole, treatment of 4,5-dihydro-3-(4-bromophenyl)-5-(methanesulfonyloxymethyl)isoxazole with NH4OH, acetylation of 4,5-dihydro-3-(4-bromophenyl)-5-(aminomethyl)isoxazole with Ac2O, and reaction of N-[4,5-dihydro-3-(4-bromophenyl)-5-isoxazolyl]acetamide with 2-methoxy-5-trimethylstannyltropone afforded the title compd. II which showed, e.g., MIC of 4 .mu.g/mL against *Staphylococcus aureus* UC No. 9213.

IT 203634-03-1P 203634-06-4P 203634-09-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of isoxazolines as antimicrobials)

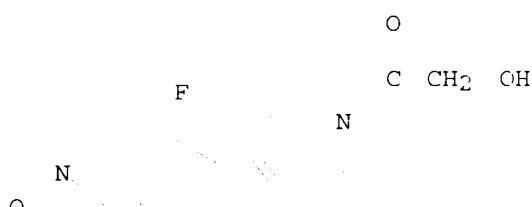
RN 203634-03-1 CAPLUS

CN Acetamide, N-[4,5-dihydro-3-[4-[2,3,6,7-tetrahydro-1-(hydroxyacetyl)-1H-azepin-4-yl]phenyl]-5-isoxazolyl]methyl] - (9CI) (CA INDEX NAME)



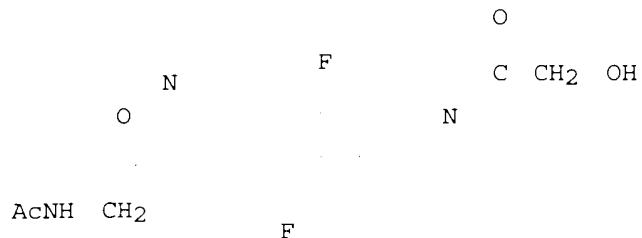
RN 203634-06-4 CAPLUS

CN Acetamide, N-[3-[3-fluoro-4-[2,3,6,7-tetrahydro-1-(hydroxyacetyl)-1H-azepin-4-yl]phenyl]-4,5-dihydro-5-isoxazolyl]methyl] - (9CI) (CA INDEX NAME)



RN 203634-09-7 CAPLUS

CN Acetamide, N-[3-[3,5-difluoro-4-[2,3,6,7-tetrahydro-1-(hydroxyacetyl)-1H-azepin-4-yl]phenyl]-4,5-dihydro-5-isoxazolyl]methyl] - (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1989:186396 CAPLUS
DN 110:186396
TI Mast cell tryptase and chymase reverse airway smooth muscle relaxation induced by vasoactive intestinal peptide in the ferret
AU Franconi, Giovanna M.; Graf, Paul D.; Lazarus, Stephen C.; Nadel, Jay A.; Caughey, George H.
CS Cardiovasc. Res. Inst., Univ. California, San Francisco, CA, 94143, USA
SO J. Pharmacol. Exp. Ther. (1989), 248(3), 947-51
CODEN: JPETAB; ISSN: 0022-3565
DT Journal
LA English
AB To explore the potential role of mast cell mediators in modulating neural control of airway tone, the effect of the mast cell proteases **tryptase** and chymase on airway smooth muscle relaxation induced by VIP was studied in the ferret airway. Tracheal rings precontracted by serotonin (10-6M) in a muscle bath were relaxed by VIP (10-7M). Protease-rich supernatant obtained by degranulation of dog mastocytoma cells reversed VIP-induced relaxation, as did highly purified **tryptase** and chymase incubated with the tracheal rings. Either enzyme completely reversed the effect of VIP, but **tryptase** was more potent than chymase, paralleling previous test tube observations on the relative rates of VIP cleavage by the two enzymes. Inhibitors of mast cell **tryptase** and chymase preincubated with the supernatant or with the purified proteases prevented reversal of VIP-induced relaxation. Mast cell proteases did not reverse the tracheal relaxation caused by the nonpeptide **adrenergic** agonist isoproterenol. Thus, the mast cell proteases **tryptase** and chymase counteract the smooth muscle relaxant effects of VIP in ferret trachea and suggest a potential role for the mast cell proteases in the modulation of nonadrenergic neural control of airway tone by VIP.

L5 ANSWER 1 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-49-5 REGISTRY
CN 3-Pyridinemethanamine, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C17 H21 N3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

N CH₂ Ph
N

CH₂ NH₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 2 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-43-9 REGISTRY
CN Benzenemethanamine, N,N-dimethyl-3-[1-(phenylmethyl)-3-pyrrolidinyl]-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C20 H26 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ NMe₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 3 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-40-6 REGISTRY
CN Benzenemethanamine, N-methyl-3-[1-(phenylmethyl)-3-pyrrolidinyl]-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H24 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ NHMe

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 4 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-36-0 REGISTRY
CN Carbamic acid, [[4-[1-(phenylmethyl)-3-pyrrolidinyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H30 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ NH C OBu-t

O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 5 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-35-9 REGISTRY
CN Carbamic acid, [[3-[1-(phenylmethyl)-3-pyrrolidinyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H30 N2 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ NH C OBu-t

O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 6 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-34-8 REGISTRY
CN Pyrrolidine, 1-(phenylmethyl)-3-[4-(phenylmethyl)phenyl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C24 H25 N
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ Ph

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 7 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-33-7 REGISTRY
CN Benzenemethanamine, 3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C18 H22 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ NH₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 8 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-32-6 REGISTRY
CN 3-Pyridinecarbonitrile, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C17 H17 N3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

N N CH₂ Ph

CN

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 9 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 150281-31-5 REGISTRY
CN Pyridine, 2-nitro-6-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI)
(CA INDEX NAME)
FS 3D CONCORD
MF C16 H17 N3 O2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

O₂N N N CH₂ Ph

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 10 OF 16 REGISTRY COPYRIGHT 2003 ACS

RN 150281-30-4 REGISTRY
CN Benzenemethanamine, N-methyl-4-[1-(phenylmethyl)-3-pyrrolidinyl]-
(9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C19 H24 N2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

CH₂ Ph

N

CH₂ NHMe

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1957 TO DATE)
1 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 11 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 145105-06-2 REGISTRY
CN Pyridine, 4-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX
NAME)
FS 3D CONCORD
MF C16 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

N

N

Ph CH₂

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 145105-05-1 REGISTRY
CN Pyridine, 3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX
NAME)
FS 3D CONCORD

MF C16 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

N

N CH₂ Ph

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1957 TO DATE)
3 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 13 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 145105-04-0 REGISTRY
CN Pyridine, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA INDEX
NAME)
FS 3D CONCORD
MF C16 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER,
USPATFULL
(*File contains numerically searchable property data)

N

N CH₂ Ph

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 14 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 145105-03-9 REGISTRY
CN Benzonitrile, 4-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN 4-[1-(Phenylmethyl)-3-pyrrolidinyl]benzonitrile
FS 3D CONCORD
MF C18 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

CH₂ Ph

N

CN

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 15 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 145105-02-8 REGISTRY
CN Benzonitrile, 3-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA
INDEX NAME)
OTHER NAMES:
CN 3-[1-(Phenylmethyl)-3-pyrrolidinyl]benzonitrile
FS 3D CONCORD
MF C18 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

CH₂ Ph

N

CN

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

L5 ANSWER 16 OF 16 REGISTRY COPYRIGHT 2003 ACS
RN 145105-01-7 REGISTRY
CN Benzonitrile, 2-[1-(phenylmethyl)-3-pyrrolidinyl]- (9CI) (CA
INDEX NAME)
FS 3D CONCORD
MF C18 H18 N2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX, TOXCENTER, USPATFULL
(*File contains numerically searchable property data)

CH₂ Ph

N

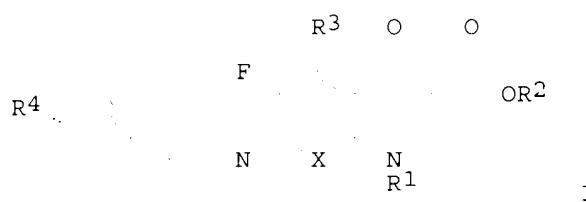
CN

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1957 TO DATE)
2 REFERENCES IN FILE CAPLUS (1957 TO DATE)

AN 1993:580755 CAPLUS
DN 119:180755
TI Preparation of 7-substituted quinolones and naphthyridones as
antibacterial agents
IN Laborde, Edgardo; Schroeder, Mel
PA Warner-Lambert Co., USA
SO U.S., 17 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
PI	US 5221676	A	19930622	US 1992-832188	19920206
	WO 9316077	A1	19930819	WO 1993-US266	19930112
	W: AU, CA, CZ, FI, HU, JP, KR, NO, NZ, PT, RU, SK				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9334701	A1	19930903	AU 1993-34701	19930112
	ZA 9300826	A	19940805	ZA 1993-826	19930205
	US 5342844	A	19940830	US 1993-14286	19930205
	US 5384407	A	19950124	US 1994-221145	19940330
	US 5446044	A	19950829	US 1994-312598	19940927
	US 5622956	A	19970422	US 1995-450090	19950525
PRAI	US 1992-832188		19920206		
	WO 1993-US266		19930112		
	US 1993-14286		19930205		
	US 1994-221145		19940330		
	US 1994-312598		19940927		
OS	MARPAT 119:180755				
CI					



AB Title compds. I (X = HC, FC, ClC, MeOC, F3CC, N; R1 = (substituted) C1-4 alkyl, -C3-6 cycloalkyl, -Ph; R2 = H, C1-4 alkyl, cation; R3 = H, H2N, Me; R4 = (substituted) methylamino), salt or quaternary ammonium salt thereof, are prep'd. 7-Chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-1,8-naphthyridine-3-carboxylic acid, 2-(3-pyrrolidinyl)benzenemethanamine (prepn. given) and EtN(CHMe₂)₂ in MeCN were refluxed for 24 h to give after recrystn. I (R1 = cyclopropyl, R2 = R3 = H, R4 = 2-H₂NCH₂, X = N) (II). II showed a min. inhibitory concn. of 0.05 .mu.g/mL against *Streptococcus faecalis*.

IT 150281-37-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(prepn. and reaction of, in prepn. of antibacterials)
RN 150281-37-1 CAPLUS
CN Benzenemethanamine, 2-(3-pyrrolidinyl)- (9CI) (CA INDEX NAME)

H
N

CH₂ NH₂

=> s tryptase(1) inhibit?
 1244 TRYPTASE
 1503214 INHIBIT?
 L1 515 TRYPTASE(L) INHIBIT?

 => s l1(L) (piperidin? or pyrrolidin?)
 72627 PIPERIDIN?
 44076 PYRROLIDIN?
 L2 16 L1(L) (PIPERIDIN? OR PYRROLIDIN?)

=> d bib abs 1-16

L2 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS
 AN 2002:594841 CAPLUS
 TI Preparation of N,N'-bis(N-alkanoyl-2-alkoxycarbonyl-4-pyrrolidinyl)-2,6-dioxoperhydro-1,5-diazocene-1,5-diacetamides and analogs as **tryptase inhibitors**
 IN Baer, Thomas; Martin, Thomas; Stadlwieser, Josef; Wollin, Stefan-Lutz; Zech, Karl; Sommerhoff, Christian P.; Ulrich, Wolf-Ruediger
 PA BYK Gulden Lomberg Chemische Fabrik GmbH, Germany
 SO PCT Int. Appl., 28 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002060895	A1	20020808	WO 2002-EP200831	20020126
	W: AE, AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR, HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
PRAI	EP 2001-102098	A	20010131		
GI					

R²

R¹ N
 O II

AB Z(CH₂CCONHR)₂ [I; R = **pyrrolidinyl** group II; R₁ = H₂NCH₂Z₁Z₂; R₂ = CO₂R₃ or CONHR₅; R₃ = H, alkyl, CH₂Ph; R₅ = H or cyclopropyl; Z = 2,6-dioxoperhydro-1,5-diazocene-1,5-diyl; Z₁ = 1,4-phenylene or -cyclohexylene; Z₂ = bond or CH₂CH₂] were prep'd. as **tryptase inhibitors** (no data). Thus, 4-(OOHC)C₆H₄CH:CHCO₂Me was converted in 3 steps to 4-(BocHNH₂C)C₆H₄CH₂CH₂CO₂H which was amidated by Me 4-azidoprolinate and the reduced product amidated by Z(CH₂CO₂H)₂ (prepn. given) to give I [R₁ = CH₂CH₂C₆H₄(CH₂NH₂)₄, R₂ = CO₂Me].
 RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS
 AN 2002:465859 CAPLUS

(97501-93-4/RN)

L2 36 (103565-40-8/BI OR 132691-45-3/BI OR 162046-58-4/BI OR 325470-40-4/BI OR 325470-41-5/BI OR 325470-45-9/BI OR 444899-38-1/BI OR 444899-40-5/BI OR 444899-42-7/BI OR 444899-44-9/BI OR 444899-46-1/BI OR 444899-49-4/BI OR 444899-53-0/BI OR 444899-55-2/BI OR 444899-60-9/BI OR 444899-62-1/BI OR 444899-64-3/BI OR 444899-66-5/BI OR 444899-68-7/BI OR 444899-70-1/BI OR 444899-72-3/BI OR 444899-74-5/BI OR 444899-76-7/BI OR 444899-78-9/BI OR 444899-80-3/BI OR 444899-84-7/BI OR 444899-85-8/BI OR 445304-16-5/BI OR 445304-17-6/BI OR 445304-18-7/BI OR 445304-19-8/BI OR 5292-43-3/BI OR 7560-50-1/BI OR 84520-69-4/BI OR 935-18-2/BI OR 97501-93-4/BI)

=> d scan

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN 2-Propenoic acid, 3-[4-[(hydroxyimino)methyl]phenyl]-, methyl ester (9CI)
 MF C11 H11 N O3

O

CH CH C OMe

HO N CH

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):10

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN L-Proline, 4-amino-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, methyl ester, (4S)- (9CI)
 MF C21 H31 N3 O5

Absolute stereochemistry.

O

t-BuO N
 H

O

O

N

S OMe

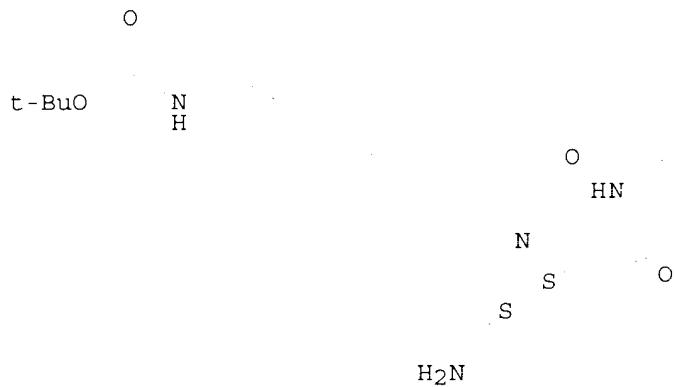
S

H₂N

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Carbamic acid, [[4-[3-[(2S,4S)-4-amino-2-[(cyclopropylamino)carbonyl]-1-pyrrolidinyl]-3-oxopropyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI)
MF C23 H34 N4 O4

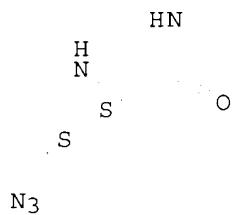
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Pyrrolidinecarboxamide, 4-azido-N-cyclopropyl-, (2S,4S)- (9CI)
MF C8 H13 N5 O

Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 2-Propenoic acid, 3-(4-formylphenyl)-, methyl ester (9CI)
MF C11 H10 O3

O

CH CH C OMe

OHC

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-1,5(2H,6H)-diacetic acid, tetrahydro-2,6-dioxo-,
bis(1,1-dimethylethyl) ester (9CI)
MF C18 H30 N2 O6

O

O CH2 C OBu-t
O N
O N
t-BuO C CH2 O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C52 H72 N8 O14

Absolute stereochemistry.

PAGE 1-A

O O
t-BuO N MeO S O N
H H S N
N S N
O

PAGE 1-B

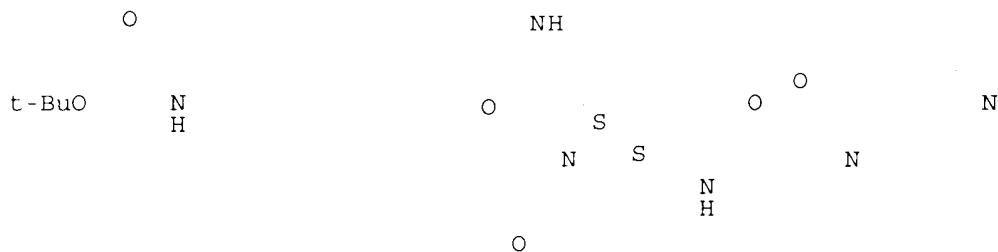
O
H N
S N
O S OMe H N OBu-t
O O
O

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

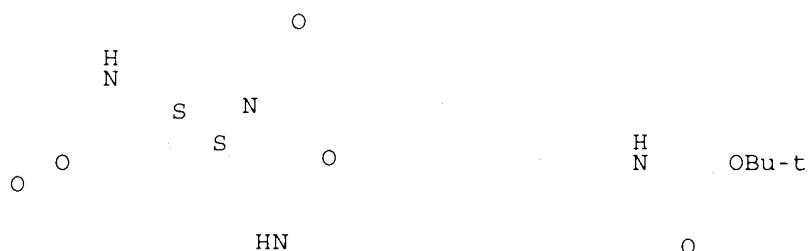
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C56 H78 N10 O12

Absolute stereochemistry.

PAGE 1-A



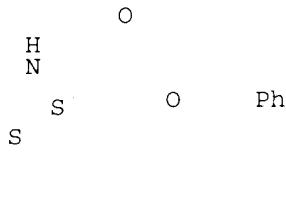
PAGE 1-B



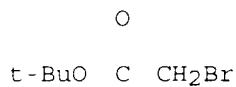
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-, phenylmethyl ester, (4S)- (9CI)
MF C12 H14 N4 O2

Absolute stereochemistry.

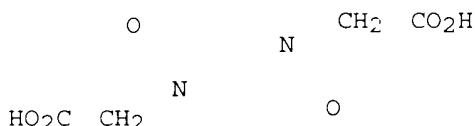


L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN Acetic acid, bromo-, 1,1-dimethylethyl ester (9CI)
 MF C6 H11 Br O2
 CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN 1,5-Diazocine-1,5(2H,6H)-diacetic acid, tetrahydro-2,6-dioxo- (9CI)
 MF C10 H14 N2 O6



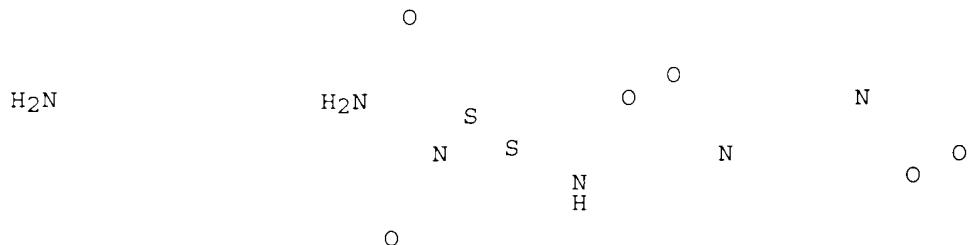
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):25

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN 1,5-Diazocine-1,5(2H,6H)-diacetamide, N,N'-bis[(3S,5S)-5-(aminocarbonyl)-1-[3-[4-(aminomethyl)phenyl]-1-oxopropyl]-3-pyrrolidinyl]tetrahydro-2,6-dioxo-, dihydrochloride (9CI)
 MF C40 H54 N10 O8 . 2 Cl H

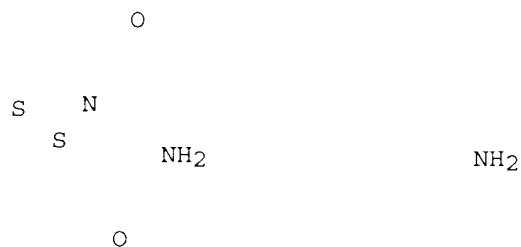
Absolute stereochemistry.

PAGE 1-A



●2 HCl

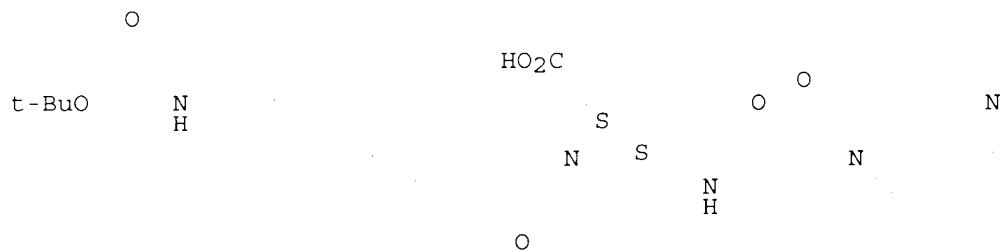
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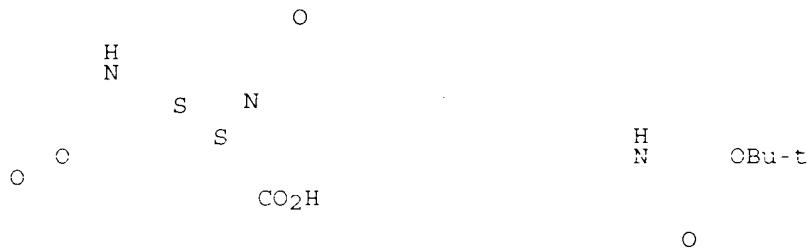
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C50 H68 N8 O14

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, (4S)- (9CI)
MF C20 H27 N5 O5

Absolute stereochemistry.

O

N OBu-t
H

O

N CO₂H
S
S

N₃

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-2,6(1H,3H)-dione, tetrahydro- (6CI, 7CI, 8CI, 9CI)
MF C6 H10 N2 O2
CI COM

H
N
O

O
N
H

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Cyclohexanecarboxylic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]- (9CI)
MF C13 H23 N O4

O

CH₂ NH C OBu-t

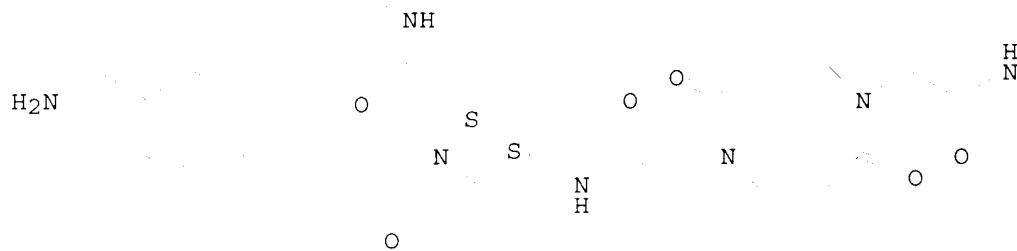
HO₂C

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN 1,5-Diazocine-1,5(2H,6H)-diacetamide, N,N'-bis[(3S,5S)-1-[3-[4-(aminomethyl)phenyl]-1-oxopropyl]-5-[(cyclopropylamino)carbonyl]-3-pyrrolidinyl]tetrahydro-2,6-dioxo-, dihydrochloride (9CI)
MF C46 H62 N10 O8 . 2 Cl H

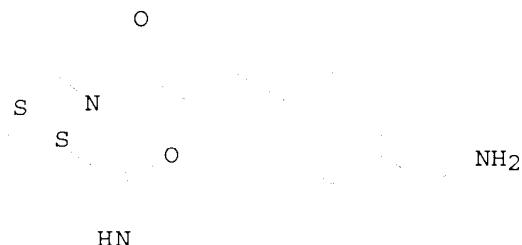
Absolute stereochemistry.

PAGE 1-A



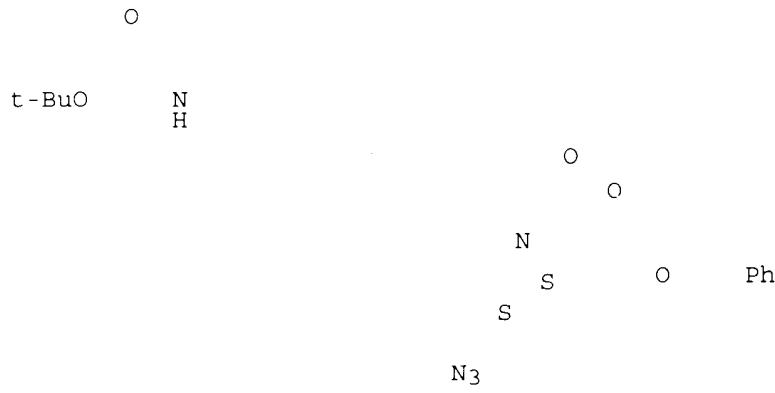
●2 HCl

PAGE 1-B



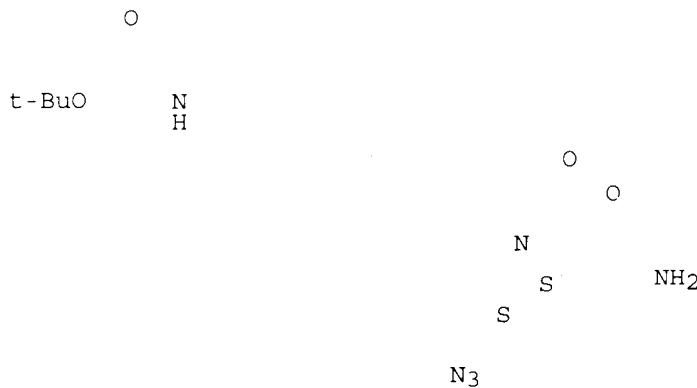
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, phenylmethyl ester, (4S)- (9CI)
MF C27 H33 N5 O5

Absolute stereochemistry.



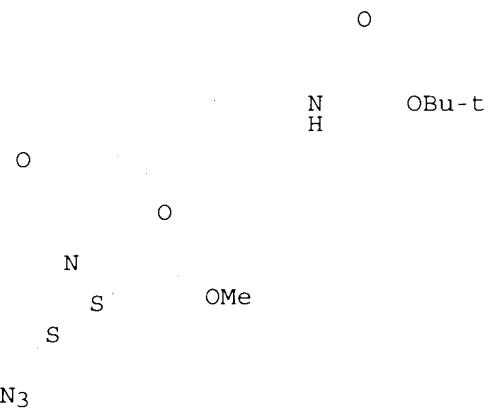
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN INDEX NAME NOT YET ASSIGNED
 MF C20 H28 N6 O4

Absolute stereochemistry.

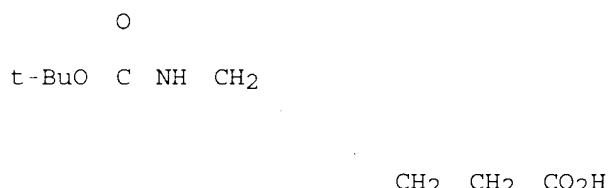


L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN L-Proline, 4-azido-1-[[4-[[[1,1-dimethylethoxy)carbonyl]amino]methyl]cycl
ohexyl]carbonyl]-, methyl ester, (4S)- (9CI)
 MF C19 H31 N5 O5

Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN Benzene propanoic acid, 4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]-
 (9CI)
 MF C15 H21 N O4

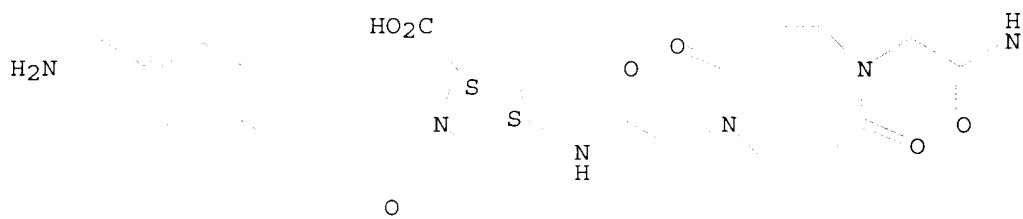


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
 IN INDEX NAME NOT YET ASSIGNED
 MF C40 H52 N8 O10 . 2 Cl H

Absolute stereochemistry.

PAGE 1-A

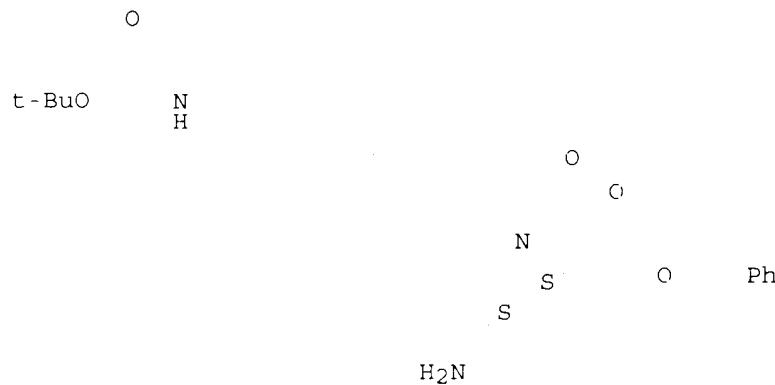


●2 HCl



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-amino-1-[3-[4-[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl-1-oxopropyl-, phenylmethyl ester, (4S)- (9CI)
MF C27 H35 N3 O5

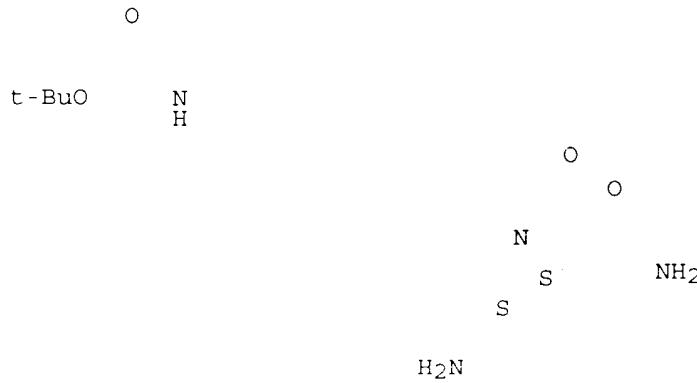
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C20 H30 N4 O4

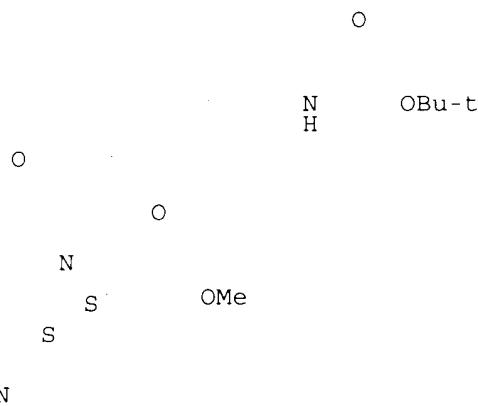
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

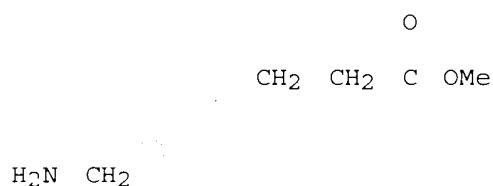
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-amino-1-[(4-[(1,1-dimethylethoxy)carbonyl]amino)methyl]cyclohexyl carbonyl, methyl ester, (4S)- (9CI)
MF C19 H33 N3 O5

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

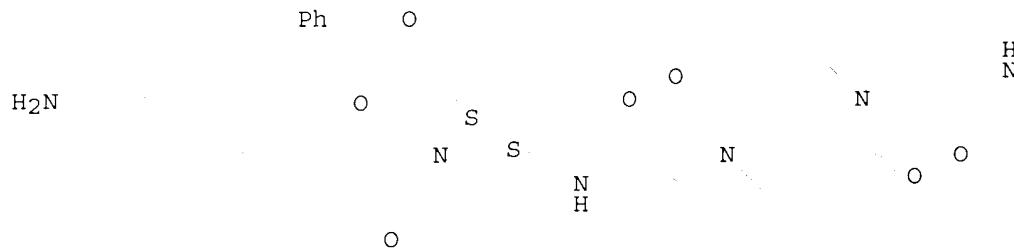
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Benzenepropanoic acid, 4-(aminomethyl)-, methyl ester, hydrochloride (9CI)
MF C11 H15 N O2 . Cl H



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
ME C54 H64 N8 O10 2 C1 H

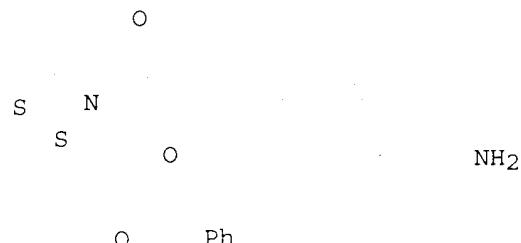
Absolute stereochemistry.

PAGE 1-A



●2 HCl

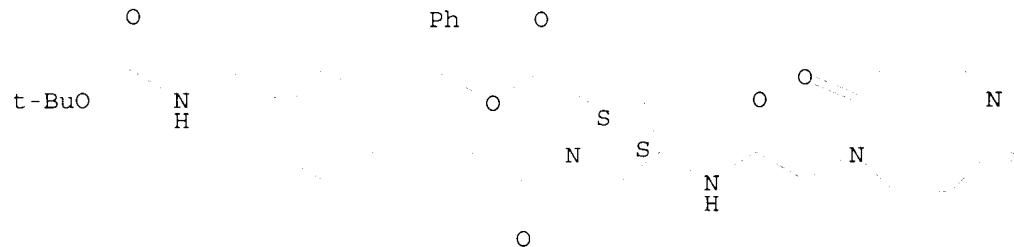
PAGE 1-B



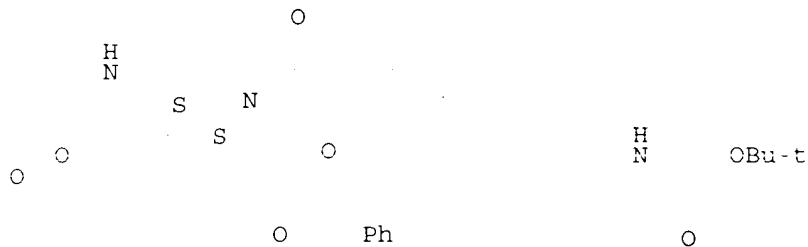
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C64 H80 N8 O14

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

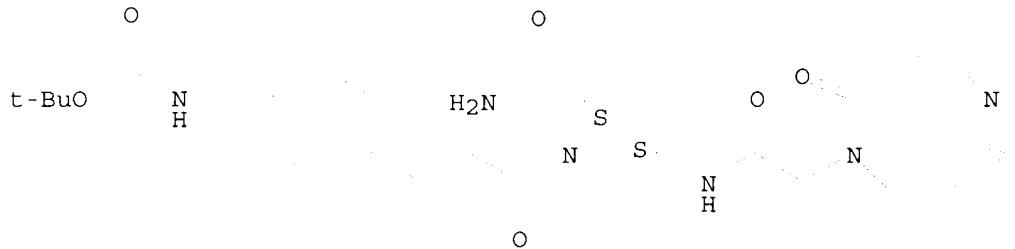


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

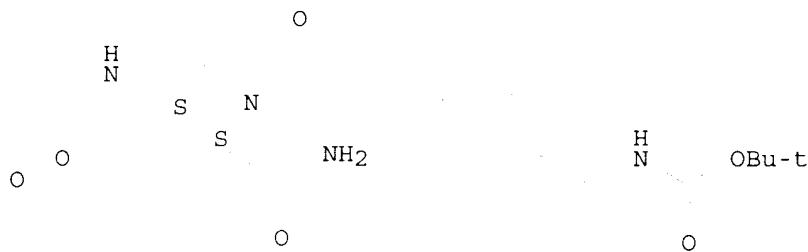
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C50 H70 N10 O12

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

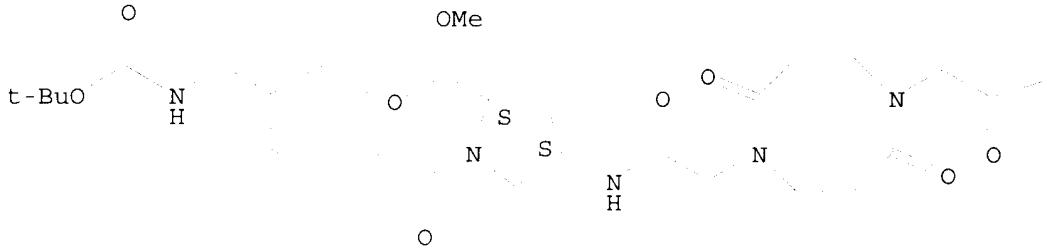


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

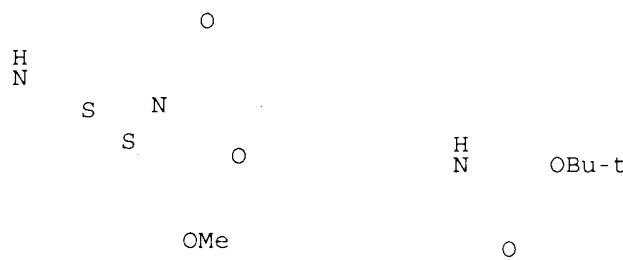
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C48 H76 N8 O14

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

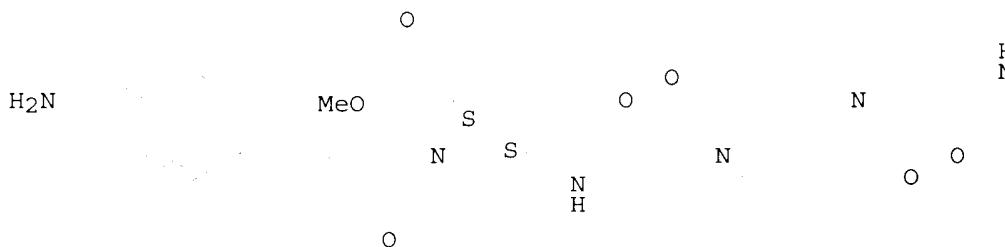
L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Tryptase (9CI)
MF Unspecified
CI MAN

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C42 H56 N8 O10 . 2 Cl H

Absolute stereochemistry.

PAGE 1-A



●2 HCl

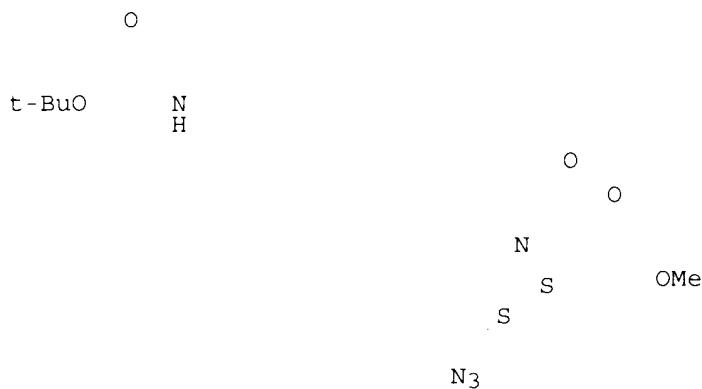
PAGE 1-B



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS

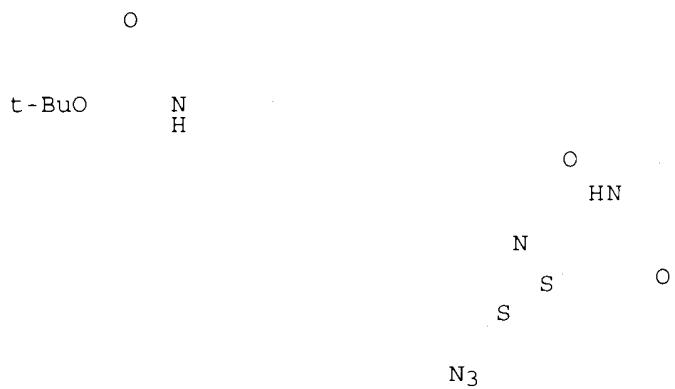
IN L-Proline, 4-azido-1-[3-[4-[[[(1,1-dimethylethoxy)carbonyl]amino]methyl]phenyl]-1-oxopropyl]-, methyl ester, (4S)- (9CI)
MF C21 H29 N5 O5

Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN Carbamic acid, [[4-[3-[(2S,4S)-4-azido-2-[(cyclopropylamino)carbonyl]-1-pyrrolidinyl]-3-oxopropyl]phenyl]methyl]-, 1,1-dimethylethyl ester (9CI)
MF C23 H32 N6 O4

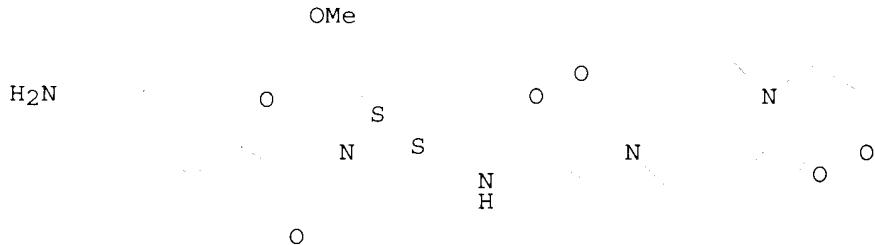
Absolute stereochemistry.



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN INDEX NAME NOT YET ASSIGNED
MF C38 H60 N8 O10 . 2 Cl H

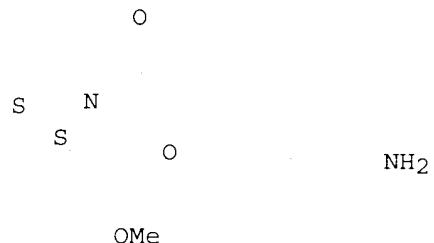
Absolute stereochemistry.

PAGE 1-A



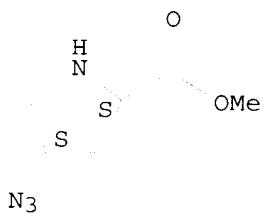
●2 HCl

PAGE 1-B



L2 36 ANSWERS REGISTRY COPYRIGHT 2002 ACS
IN L-Proline, 4-azido-, methyl ester, (4S)- (9CI)
MF C6 H10 N4 O2
CI COM

Absolute stereochemistry.



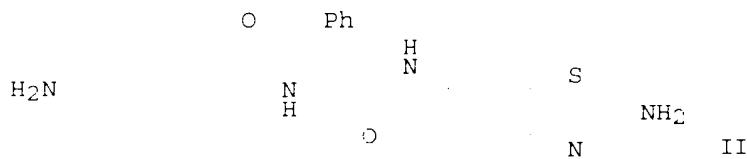
ALL ANSWERS HAVE BEEN SCANNED

DN 137:47190
 TI Preparation of (fused) thiazolyl and thieryl-substituted
 N-(aminomethylbenzoyl) (hetero)arylglycinamides as tryptase inhibitors.
 IN Lively, Sarah Elizabeth; Harrison, Martin James; Naylor, Neil Jason;
 Farthing, Christopher Neil; Waszkowycz, Bohdan
 PA Tularik Limited, UK
 SO PCT Int. Appl., 138 pp.
 CODEN: PIIXXD2
 DT Patent
 LA English
 FAN.CNT 12

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002047762	A1	20020620	WO 2001-GB5526	20011212
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	WO 2001044226	A1	20010621	WO 2000-GB4764	20001213
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	WO 2000-GB4764	W	20001213		
	GB 2001-14185	A	20010612		
	GB 1999-29552	A	19991214		
	WO 2000-GB2291	W	20000613		
OS	MARPAT 137:47190				
GI					

R5 CY
X CH L Lp

H₂N R⁶



AB N-(3-aminomethylbenzoyl)aryl- and heteroaryl glycinamides I [Cy = (un)substituted cycloalkyl, aryl, heterocyclyl, heteroaryl; L = CONR1(CH2)m; Lp = (un)substituted thiazolyl, thiazol-2-yl, 4-arylthiazol-2-yl, benzothiazol-2-yl, 4,5,6,7-tetrahydrobenzothiazol-2-yl, etc.; m = 0, 1; R1 = H, alkyl, phenylalkyl; R5 = H, H2N, HO, H2NCH2, HOCH2; R6a = H, Me; X = CH:CH, CONR1, NHCO, NR1CH2, CH2O, CO2, CH2CH2] are prepd. as inhibitors of the serine protease tryptase for the treatment of asthma (no data). E.g., 2,6-diaminobenzothiazole (prepd. by redn. of 2-amino-6-nitrobenzothiazole) was coupled with N-Boc-D-phenylglycine, deprotected with F3CCO2H, the free .alpha.-amino group coupled with 3-(N-tert-butoxycarbonylaminomethyl)benzoic acid, and the product deprotected with F3CCO2H to give phenylglycinamide II. Formulations contg. I are given.

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2002:389878 CAPLUS
TI Anti-inflammatory 1-aryl-4-(m-aminomethylphenyl)piperidine derivatives
AU Anon.
SO Expert Opinion on Therapeutic Patents (2002), 12(5), 751-754
CODEN: EOTPEG; ISSN: 1354-3776
PB Ashley Publications Ltd.
DT Journal
LA English
AB A series of 1-aryl-4-(m-aminomethylphenyl)**piperidine** derivs. and their 1-heteroaryl analogs are claimed. These amines are low mol. wt. **inhibitors of tryptase**, some of which have reasonable potency. If combined with good pharmacokinetic properties this class of compds. may prove to be therapeutically useful in the treatment of asthma or allergic rhinitis.

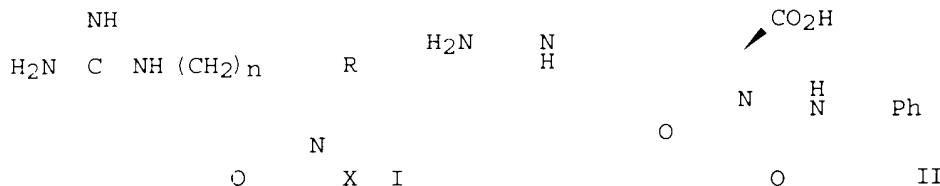
RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2002:6377 CAPLUS
DN 136:69695
TI Preparation of .beta.-lactam compounds as inhibitors of tryptase
IN Bisacchi, Gregory S.; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Schwinden, Mark D.; Xu, Zhongmin; Shi, Zhongping
PA Bristol-Myers Squibb Co., USA
SO U.S., 171 pp., Cont.-in-part of U. S. Ser. No. 336,253, abandoned.
CODEN: USXXAM
DT Patent
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6335324	B1	20020101	US 1999-458847	19991213
PRAI	US 1998-90636P	P	19980625		
	US 1999-336253	B2	19990618		
OS	MARPAT 136:69695				
GI					

NH.TFA



AB Novel .beta.-lactam compds., e.g. of formula I [R = CO₂H, alkoxy carbonyl, acyl, CO-heterocyclyl, etc.; X = acyl, CO-heterocyclyl, SO₂-alkyl, aminoalkylphenyl, etc.; n = 1-6], are prep'd. These compds. inhibit trypsin as well as other enzyme systems or are selective trypsin inhibitors and are useful as antiinflammatory agents particularly in the treatment of chronic asthma (no data). Thus, II was prep'd. from (4S)-N-(tert-butyldimethylsilyl)azetidin-2-one-4-carboxylic acid, 1-chloro-3-iodopropane, N,N'-bis(benzyloxycarbonyl)-1-guanylpyrazole and benzyl isocyanate.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as **trypsin inhibitors**
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIKXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
OS	MARPAT	136:5917			
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

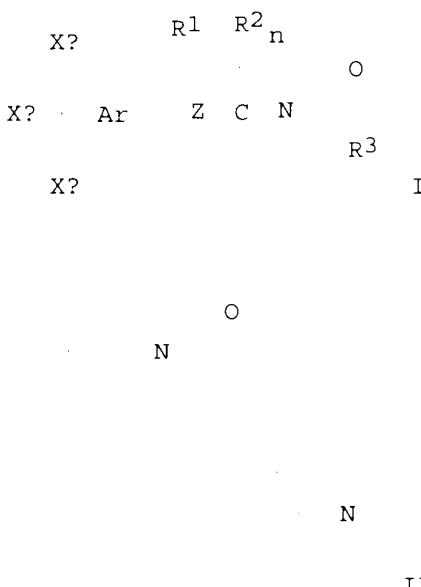
AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R₁₋₂ = H, alkyl; R₃ = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R₄ = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 -

4] were prep'd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NET, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:798195 CAPLUS
DN 135:344381
TI Preparation of 1-arylpiperidinyl benzamidines as
inhibitors of Factor Xa or tryptase
IN Pauls, Heinz; Gong, Yong; Levell, Julian; Astles, Peter C.; Eastwood, Paul
R.
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001081310	A1	20011101	WO 2001-US13810	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002045613	A1	20020418	US 2001-841417	20010424
PRAI	US 2000-200066P	P	20000427		
	GB 2000-18306	A	20000726		
OS	MARPAT	135:344381			
GI					



AB The title compds. [I; Z = C, N; ring C = 4-7 membered azaheterocyclyl, 4-7 membered azaheterocyclenyl; Ar = aryl, monocyclic heteroaryl, bicyclic azaheteroaryl; R1 = H, CH₂OR₁₂, CH₂SR₁₂, etc.; R2 = H, alkyl, aralkyl, etc.; R3 = cycloalkyl, cycloalkenyl, heterocyclyl, etc.; X_a, X_b, X_c = H, (hydroxy)NH, halo, etc.; R₁₂ = H, alkyl, acyl, etc.], useful for the treatment of patients suffering from conditions which can be ameliorated by the administration of an inhibitor of Factor Xa or tryptase, were prepd. E.g., a multi-step synthesis of II.2F3CCO₂H which showed Ki of 9.0 nM against Factor Xa, was given.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:478090 CAPLUS
DN 135:298146
TI Dibasic inhibitors of human mast cell tryptase. Part 3: Identification of a series of potent and selective inhibitors containing the benzamidine functionality
AU Dener, J. M.; Rice, K. D.; Newcomb, W. S.; Wang, V. R.; Young, W. B.; Gangloff, A. R.; Kuo, E. Y.-L.; Cregar, L.; Putnam, D.; Wong, M.
CS Departments of Medicinal Chemistry, Biochemistry, and Enzymology, Axys Pharmaceuticals, Inc., South San Francisco, CA, 94080, USA
SO Bioorganic & Medicinal Chemistry Letters (2001), 11(13), 1629-1633
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB A survey of charged groups and linkers for a series of sym. and unsym. dibasic inhibitors is described, leading to several classes of potent and selective inhibitors. The inhibitors synthesized and tested were related to the known inhibitor APC-1390. In particular, the benzamidine functionality was identified as the most potent charged group investigated.

RE.CNT 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:472693 CAPLUS
DN 135:76895

TI Preparation of tryptase inhibiting alkynediol piperazinecarboxylate esters
IN Baer, Thomas; Stadlwieser, Josef; Ulrich, Wolf-Ruediger; Dominik, Andreas;
Bundschuh, Daniela; Zech, Karl; Sommerhoff, Christian; Martin, Thomas
PA Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany
SO PCT Int. Appl., 35 pp.
COPEN: P1XXP2

CODEN: PIXXD2

DT Patent
EN English

LA English
EAN CNT 1

FAN.CN1 1

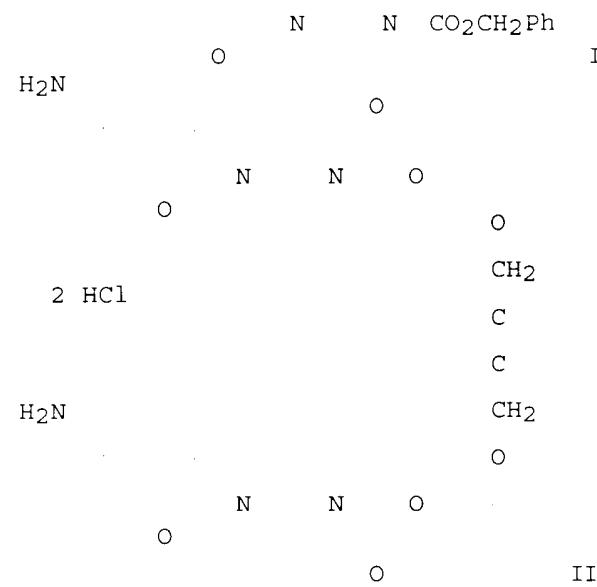
PI WO 2001046168 A1 20010628 WO 2000-EP12838 20001216
W: AE, AL, AU, BA, BG, BR, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN,
JP, KR, LT, LV, MK, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR

PRAI EP 1999-125384 A 19991220

OS MARPAT 135:76895

GI

Boc NH



AB Alkynes K2-A2-U2(C.tplbond.C)nU1-A1-K1 [n = 1, 2; U1, U2 = CH₂, CH₂CH₂, CH₂CH₂CH₂, CH₂CH₂CH₂CH₂, Me₂C; A1 = A3-B1-A5; A2 = A4-B2-A6; A3, A4 = CO, CO₂, CONH, NHCO, OCONH, NHCO₂, NHCONH, OCO₂, O(CH₂)pCO, O(CH₂)^mOCO, O(CH₂)^mNHCO; p, m = 1, 2, 3, 4; A5, A6 = CO, CONH, NHCO, OCONH, NHCO₂, NHCONH, OCO₂; B1, B2 = alkylene, cyclohexylene, phenylene, piperazinylene, **piperidinylene**; K1 = B3-X1, B3-Y1, B3-Z1-B5-X1; K2 = B4-X2, B4-Y2, B4-Z2-B6-X2; B3, B4 = bond, alkylene; B5, B6 = bond alkylene; X1, X2 = H₂N, H₂NCO, amidino; Y1, Y2 = imidazolyl; Z1, Z2 = pyridinylene, 6-methyl-5,2-pyridinylene, **piperidinylene**, 3,6-indazolylene, 3,6-indolylene, phenylene, cyclohexylene] and their salts and N-oxides were prep'd., possessed **tryptase inhibiting** activities, and were medicaments for the treatment of airway (pulmonary) disorders.

Thus, condensation of trans-4-[(tert-butoxycarbonylamino)methyl]cyclohexanecarboxylic acid and 1-(benzyloxycarbonyl)piperazine in CH₂Cl₂ contg. 1-hydroxybenzotriazole gave the (cyclohexylcarbonyl)piperazinecarboxylate I. Debenzylolation of I and subsequent esterification with 1,4-bis(2-hydroxyethoxy)-2-butyne and deblocking gave the bis(cyclohexylcarbonylpiperazinecarboxylate) ester salt II which possessed an apparent dissocn. const. of 0.086 .mu.M for its **tryptase-inhibitor** complex.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2001:454760 CAPLUS
DN 135:165939
TI Tryptase-induced airway microvascular leakage in guinea pigs: involvement of tachykinins and leukotrienes
AU Greenfeder, Scott; Sehring, Susan; McHugh, Nansie; Corboz, Michel; Rivelli, Maria; Anthes, John C.; Billah, Motasim; Egan, Robert W.; Chapman, Richard W.
CS Department of Allergy, Schering-Plough Research Institute, Kenilworth, NJ, 07033, USA
SO European Journal of Pharmacology (2001), 419(2/3), 261-267
CODEN: EJPHAZ; ISSN: 0014-2999
PB Elsevier Science B.V.
DT Journal
LA English
AB **Tryptase**, a serine protease synthesized by and stored in mast cells, is implicated as an important mediator in the pathogenesis of airway inflammation. In this study, **tryptase** was evaluated for its ability to induce microvascular leakage into the airways of guinea pigs. Dose- and time-dependent increases in airway microvascular leakage were produced by intratracheal **tryptase** (0.3-3 .mu.g). Intratracheal **tryptase** (3-30 .mu.g) had no effect on airway tone as measured by pulmonary insufflation pressure. **Tryptase**-induced airway microvascular leakage was partially blocked by the tachykinin NK1 receptor antagonist CP 99994 [(+)-(2S,3S)-3-(2-methoxybenzylamino)-2-phenylpiperidine] and an **inhibitor** of leukotriene formation SCH 37224 (1-(1,2-dihydro-4-hydroxy-2-oxo-1-phenyl-1,8-naphthyridin-2-yl)**pyrrolidinium**, hydroxide inner salt). Neither CP 99994 nor SCH 37224 **inhibited tryptase** proteolytic activity in-vitro. Pretreatment of guinea pigs with histamine H1 receptor antagonists or a tachykinin NK2 receptor antagonist had no affect on the airway microvascular leakage induced by **tryptase**. It is speculated that **tryptase** may be important in the pathogenesis of airway inflammation, particularly in disorders that involve increased airway microvascular leakage such as asthma.

RE.CNT 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2000:535126 CAPLUS
DN 133:150919
TI Preparation of peptidyl heterocyclic ketones useful as tryptase inhibitors
IN Costanzo, Michael J.; Maryanoff, Bruce E.; Yabut, Stephen C.
PA Ortho-McNeil Pharmaceutical, Inc., USA
SO PCT Int. Appl., 81 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI WO 2000044733	A1	20000803	WO 2000-US883	20000113

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
 CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
 MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
 SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
 AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1147097 A1 20011024 EP 2000-909902 20000113
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 BR 2000007778 A 20020604 BR 2000-7778 20000113
 NO 2001003666 A 20010926 NO 2001-3666 20010726
 PRAI US 1999-117602P P 19990127
 WO 2000-US883 W 20000113
 OS MARPAT 133:150919
 AB Peptidyl heterocyclic ketones A-NR₁R₂CO-E [A = substituted cycloalkylcarbonyl, norbornanecarbonyl, norbornenecarbonyl, adamantanecarbonyl, arylcarbonyl, heteroarylcarbonyl, aminoalkylcarbonyl, an amino acid or dipeptide residue, etc.; R, R₁ = H, alkyl; R₂ = amino-, guanidino-, alkylguanidino-, dialkylguanidino-, amidino-, alkylamidino-, dialkylamidino-, or alkoxyalkyl, (un)substituted Ph, benzyl, pyridyl, pyridyl-, pyrimidyl-, triazinyl-, or imidazoalkyl, imidazolinyl-, N-amidinopiperazinyl-, hydroxy-, alkylamino-, dialkylamino-, N-amidinopiperidinyl-, or 4-aminocyclohexylalkyl; E = (un)substituted heterocyclyl] and their pharmaceutically acceptable salts and prodrugs were prep'd. as **tryptase inhibitors** and are therefore effective for the prevention and treatment of inflammatory diseases assoc'd. with the respiratory tract, such as asthma and allergic rhinitis. Thus, (2S,4R)-1-acetyl-N-[(1S)-4-[(aminoiminomethyl)amino]-1-(2-benzothiazolylcarbonyl)butyl]-4-hydroxy-2-**pyrrolidinecarboxamide** was prep'd. by a seven-step procedure starting from Boc-Arg(Ts)-OH (Boc, tert-butoxycarbonyl, Ts = tosyl), benzothiazole, and trans-1-acetyl-4-benzyloxyl-L-proline and showed IC₅₀ = 0.036 .+- .0.031 .μ.M for **inhibition of trypsin**.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

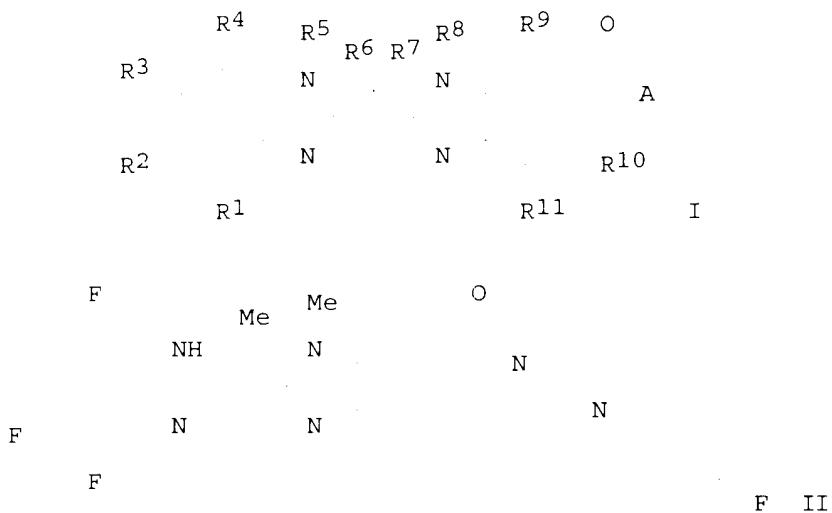
L2 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS
 AN 2000:445771 CAPLUS
 DN 133:248787
 TI Selective inhibition of trypsin by (2R,4R)-4-phenyl-1-[N.α.-(7-methoxy-2-naphthalenesulfonyl)-L-arginyl]-2-piperidinecarboxylic acid
 AU Hijikata-Okunomiya, Akiko; Tamao, Yoshikuni; Kikumoto, Ryoji; Okamoto, Shosuke
 CS Faculty of Health Science, Kobe University School of Medicine, Kobe, 654-0142, Japan
 SO Journal of Biological Chemistry (2000), 275(25), 18995-18999
 CODEN: JBCHA3; ISSN: 0021-9258
 PB American Society for Biochemistry and Molecular Biology
 DT Journal
 LA English
 AB Evidence is accumulating indicating that trypsin stimulates divergent cellular reactions through the proteinase-activated receptor, in addn. to its role as the digestive enzyme. In this report, we introduce (2R,4R)-4-phenyl-1-[N.α.-(7-methoxy-2-naphthalenesulfonyl)-L-arginyl]-2-piperidinecarboxylic acid as a potent and selective trypsin **inhibitor**. The agent **inhibited** trypsin competitively with the Ki value of 0.1 .μ.M. It **inhibited** thrombin weakly (Ki = 2 .μ.M) and did not **inhibit** plasmin, plasma kallikrein, urokinase, and mast cell **tryptase** (Ki values for these enzymes are >60 .μ.M). Comparative studies with several established proteinase

inhibitors revealed that the compd. was the first small mol. wt. trypsin **inhibitor** without **tryptase inhibitory** activity. A docking study has provided a plausible explanation for the mol. mechanism of the selective **inhibition** showing that the agent fits into the active site of trypsin without any severe collision but that it comes into clash at the 4-Ph group of **piperidine** ring against the "60-insertion loop" of thrombin and at the 7-methoxy-2-naphthalenesulfonyl group against Gln98 of **tryptase**.

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 2000:241202 CAPLUS
DN 132:265195
TI Preparation of bis-benzimidazoles as tryptase inhibitors
IN Mittendorf, Joachim; Henning, Rolf; Raddatz, Siegfried; Schlemmer, Karl-heinz; Hiraoka, Makiko; Kadono, Hiroshi; Mogi, Muneto; Moriwaki, Toshiya; Murata, Toshiki; Sakakibara, Sachiko; Shimada, Mitsuyuki; Yoshida, Nagahiro; Yoshino, Takashi
PA Bayer Yakuhin, Ltd., Japan; et al.
SO PCT Int. Appl., 140 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020401	A1	20000413	WO 1999-JP5319	19990929
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9959981	A1	20000426	AU 1999-59981	19990929
	EP 1117651	A1	20010725	EP 1999-969935	19990929
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002526537	T2	20020820	JP 2000-574518	19990929
PRAI	US 1998-102711P	P	19981001		
	US 1999-117269P	P	19990126		
	US 1999-123277P	P	19990309		
	WO 1999-JP5319	W	19990929		
OS	MARPAT	132:265195			
GI					



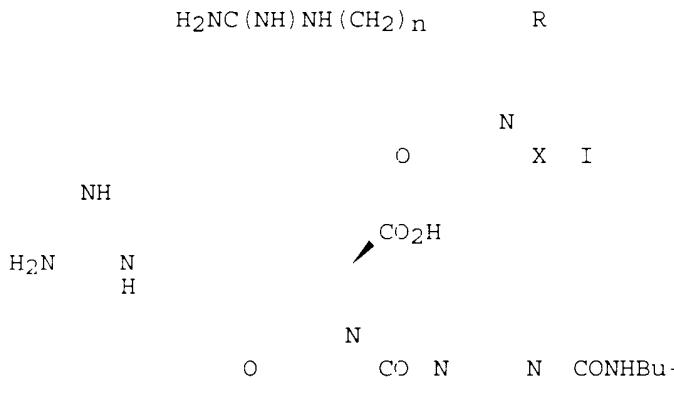
AB Title compds. (I) [wherein R1, R2, R3, and R4 = independently H, OH, or halogen; R5 and R8 = independently H or alkyl; R6 and R7 = independently H, OH, halogen, alkyl, or alkoxy; R9, R10, and R11 = independently H, halogen, NO₂, CN, or CF₃; A = non-arom. 5-7-membered N-heterocycle, etc.] were prep'd. for use in the treatment of diseases assocd. with tryptase activity including allergic, inflammatory, and related immunol. diseases, in particular asthma, allergic rhinitis, allergic conjunctivitis, and allergic dermatitis. Examples include syntheses for 70 compds. and their intermediates, tryptase inhibitory activity data, and bioavailability data. For instance, refluxing Et 2-(4,6,7-trifluoro-1H-benzimidazol-2-yl)propionate (prepn. given) with 4-amino-3-(methylamino)benzoic acid in DMPU produced the bis-benzimidazole (66%). Subsequent reaction with 1-(4-fluorophenyl)piperazine in the presence of N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide.HCl, 1-hydroxybenzotriazole, and TEA in DMF yielded II (73%). II gave a Ki of 3.0 nM in the presence of ZnCl₂ in a human tryptase inhibition assay. Compared to a known tryptase inhibitor, II showed improved oral bioavailability in rats, dogs, and primates in pharmacokinetics tests (72% vs. 0.3%, 74% vs. 0.2-7%, and 100% vs. not detd., resp.).

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1999:819347 CAPLUS
DN 132:64103
TI Preparation of amidino and guanidino azetidinone compounds as tryptase inhibitors
IN Bisacchi, Gregory; Slusarchyk, William A.; Treuner, Uwe; Sutton, James C.; Zahler, Robert; Seiler, Steven; Kronenthal, David R.; Randazzo, Michael E.; Xu, Zhongmin; Shi, Zhongping; Schwinden, Mark D.
PA Bristol-Myers Squibb Co., USA
SO PCT Int. Appl., 326 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9967215	A1	19991229	WO 1999-US13811	19990618
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,				

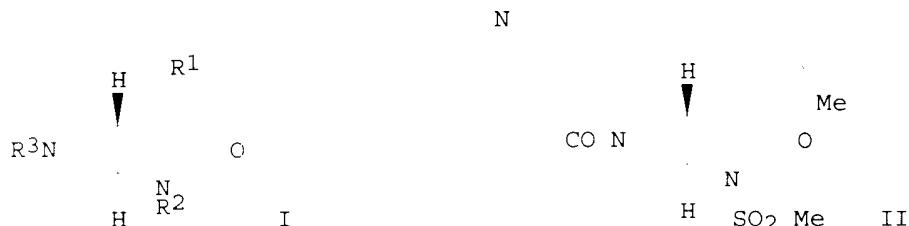


AB Novel .beta.-lactam compds., e.g. of formula I [R - CO₂H, CONH-alkyl, etc.; X = CONH(CH₂)₂NHCO₂alkyl, etc.; n = 1-6;], are prep'd. as inhibitors of in vivo enzyme systems including tryptase, thrombin, trypsin, factor Xa, factor VIIa, and urokinase-type plasminogen activator (no data). The tryptase activity makes the title compds. useful as antiinflammatory agents in the treatment of chronic asthma and allergic rhinitis. Thus, II was prep'd. from (4S)-N-(tert-butyldimethylsilyl)azetidin-2-one-4-carboxylic acid, tert-butyl-1-piperazine carboxylate and tert-Bu isocyanate.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1999:194149 CAPLUS
DN 130:223259
TI Preparation of pyrrolopyrrolidine derivatives and their use as serine protease inhibitors
IN Coote, Steven John; Dowle, Michael Dennis; Finch, Harry; Hann, Michael Menteith; Kelly, Henry Anderson; MacDonald, Simon John Fawcett; Pegg, Neil Anthony; Ramsden, Nigel Grahame; Watson, Nigel Stephen
PA Glaxo Group Limited, UK
SO PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

PI	WO 9912935	A1	19990318	WO 1998-EP5744	19980907
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9896243	A1	19990329	AU 1998-96243	19980907
	EP 1015456	A1	20000705	EP 1998-950011	19980907
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2001515906	T2	20010925	JP 2000-510742	19980907
PRAI	GB 1997-19161	A	19970909		
	WO 1998-EP5744	W	19980907		
OS	MARPAT 130:223259				
GI					

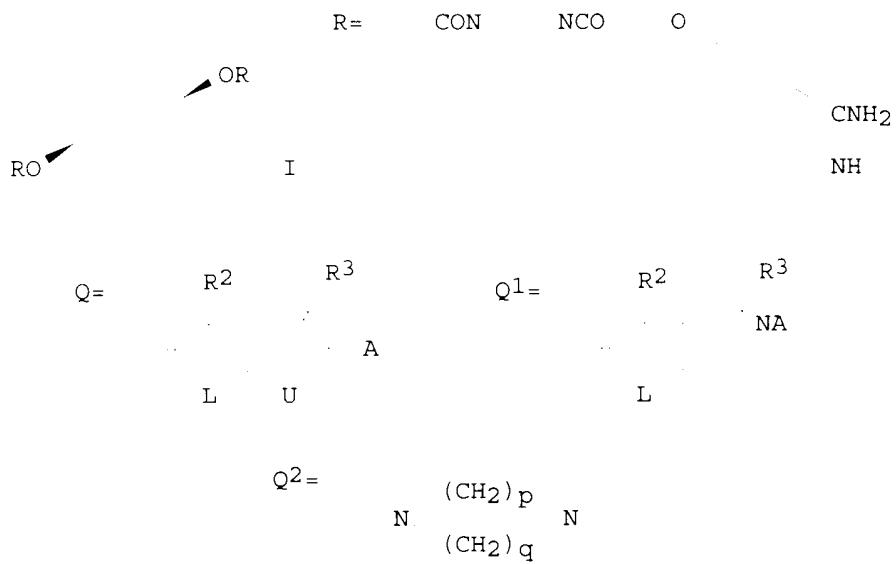


AB Trans-hexahydropyrrolo[3,4-b]pyrrol-2-ones I [R1 = moiety adapted to fit the S1 specificity subsite of the enzyme; R2 = moiety adapted to optimize potency, pharmacokinetics, pharmacodynamics, selectivity, and enzyme kinetics; R 3 = moiety adapted to optimize potency, pharmacokinetics, pharmacodynamics, and physicochem. properties] were prep'd. as antiviral serine protease **inhibitors**. Thus, the hydrochloride salt of trans-hexahydropyrrolo[3,4-b]pyrrol-2-one II was prep'd. starting from trans-4-nitro-1-(phenylmethyl)-3-pyrrolidineacetic acid Et ester, allyl iodide, and 4-(piperidin-1-yl)-but-2-enoic acid hydrochloride. The prep'd. compds. were tested for **inhibition** of viral serine protease, human mast cell **tryptase**, trypsin, tissue plasminogen activator, Factors VIIa, Xa, XIIa, XIIa, plasmin, chymotrypsin, and cathepsin G.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1999:194135 CAPLUS
DN 130:237590
TI Preparation of bis(piperazin-1-ylcarbonylmethoxy)cyclooctane and -benzene and related derivatives as selective tryptase inhibitors
IN Ono, Shinichiro; Takeuchi, Masahiro; Sakashita, Hiroshi; Kuwahara, Shigeki; Naito, Koji; Naito, Youichiro; Imagawa, Takashi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1
PATENT NO. KIND DATE APPLICATION NO. DATE

 PI WO 9912918 A1 19990318 WO 1998-JP3978 19980904
 W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
 DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
 KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO,
 NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA,
 UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 AU 9889974 A1 19990329 AU 1998-89974 19980904
 PRAI JP 1997-241387 19970905
 WO 1998-JP3978 19980904
 OS MARPAT 130:237590
 GI



AB Claimed are compds. represented by general formula of
 $ZCOYCO(CH_2)_nXWY_1(CH_2)_nCOY_1COZ_1$ [Z, Z₁ = Q, Q₁; wherein A = E₁E₁₁NC(:NE₂), E₁E₁₁NC(:NE₂)NE₃, E₁E₁₁N(CH₂)_d, E₁E₁₁NCO; E₁, E₁₁, E₂, E₃ = H, aralkyl, alkyl, amidino, guanidino, protecting group for primary amino group; E₂ is addnl. OH; or E₁E₁₁N = heterocyclyl contg. addnl. heteroatoms; d = 1-3; Z, Z₁ = E₁E₁₁C(:NE₂), E₁E₂N (CH₂)_d (d = 1,3); L = O, NR₄, S, SO₂, CH₂; R₄ = H, alkyl, cycloalkyl, aralkyl, acyl; U = :CH, :N; R₂, R₃ = H, alkyl, halo, CF₃, OH, NH₂, acyl, alkoxy; W = (CH₂)_l (l = 1-10), (un)substituted C₃-14 cycloalkylene; Y, Y₁ = Q₂ (p, q = 1-3), NH(CH₂)_cNH (c = 1-8); n, n₁ = 0,1] or pharmacol. acceptable salts thereof, a pharmaceutical compn. thereof, and use thereof as a pharmaceutical, in particular a tryptase inhibitor and allergy inhibitor based on tryptase inhibition activity. The compds. and pharmacol. acceptable salts thereof have an excellent tryptase inhibitory activity with high selectivity, are orally administrable, and have a reduced toxicity, thus being useful for pharmaceuticals, for example, those for prophylaxis or therapy of allergic diseases such as allergic rhinitis, hypersensitive pneumonia, pulmonary fibrosis, and bronchial asthma. Thus, cis-1,5-bis(piperazin-1-ylcarbonyloxy)cyclooctane dihydrochloride was condensed with 5-[1-(benzyloxycarbonylamino)-1-iminomethyl]benzofuran-2-ylcarboxylic acid using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, HOEt, and Et₃N in DMF for 17 h, followed by hydrogenolysis over 10% Pd-C in CHCl₃/MeOH to give the

title compd. (I).2HCl. I.2HCl inhibited human tryptase and human thrombin with Ki of 2.5 .times. 10-12 and 4.5 .times. 10-5 M, resp.

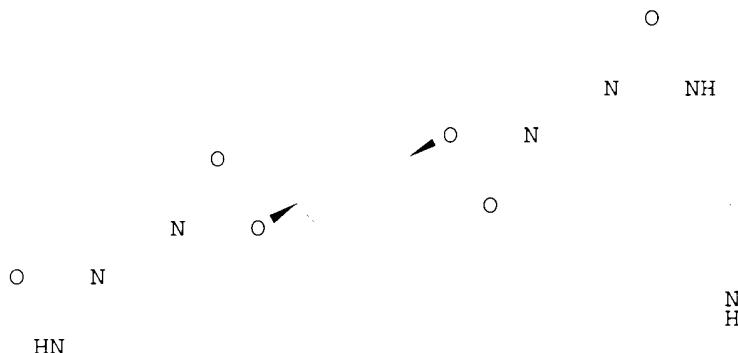
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS
AN 1998:102855 CAPLUS
DN 128:167443
TI Novel compounds [cyclooctylene bis(piperazinecarboxylates) and analogs] and compositions for treating diseases associated with tryptase activity
IN Dener, Jeffrey Mark; Kuo, Elaine Yee-Lin; Rice, Ken Duane; Wang, Vivian Rueywen; Young, Wendy Beth
PA Arris Pharmaceutical Corporation, USA; Dener, Jeffrey Mark; Kuo, Elaine Yee-Lin; Rice, Ken Duane; Wang, Vivian Rueywen; Young, Wendy Beth
SO PCT Int. Appl., 100 pp.
CODEN: PIXXD2

DT Patent
LA English

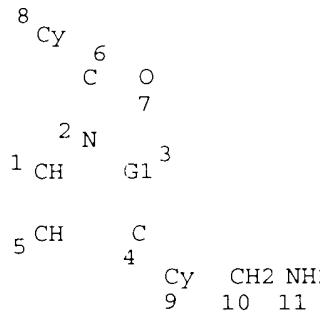
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9804537	A1	19980205	WO 1997-US13422	19970730
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9739670	A1	19980220	AU 1997-39670	19970730
	AU 733621	B2	20010517		
	EP 934293	A1	19990811	EP 1997-937066	19970730
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1226892	A	19990825	CN 1997-196877	19970730
	CN 1073103	B	20011017		
	JP 2001509787	T2	20010724	JP 1998-509136	19970730
	FI 9900171	A	19990323	FI 1999-171	19990129
	NO 9900433	A	19990325	NO 1999-433	19990129
	KR 2000029679	A	20000525	KR 1999-7000757	19990129
	LV 12291	B	20000420	LV 1999-27	19990218
	LT 4587	B	19991227	LT 1999-19	19990301
	LV 12458	B	20000920	LV 2000-30	20000225
	LV 12459	B	20000920	LV 2000-31	20000225
PRAI	US 1996-23139P	P	19960730		
	US 1997-895772	A	19970717		
	US 1996-23139	A	19960730		
	WO 1997-US13422	W	19970730		
	LV 1999-990027	A3	19990218		
OS	MARPAT	128:167443			
GI					



AB The invention relates to novel compds. (R₁X₁X₂X₃X₄) -X₅- (X₆X₇X₈X₉R₂) (I), which are **tryptase inhibitors**, and their pharmaceutically acceptable salts and N-oxides, as well as their uses as therapeutic agents, and methods of their prepn. [wherein X₅ = (hetero)cycloalkylene, (hetero)arylene; X₄, X₆ = bond, alkylene; X₁, X₉ = bond, CO, CO₂, OCO, CONR₃, NR₃CO, etc.; R₃ = H, alkyl, cycloalkyl; X₃, X₇ = CO, CO₂, OCO, CONR₃, NR₃CO, etc.; X₂, X₈ = (hetero)alkylene and/or cycloalkylene; R₁ = amino, amidino, guanidino, certain N-heterocycles, etc., with optional (hetero)alkylene or other bridge; R₂ = amino, 1-iminoethyl, methylamino, or certain N-heterocycles, with required or optional alkylene or other bridge]. The compds. are useful for treating a variety of conditions, including asthma, rheumatoid arthritis, and conjunctivitis. For instance, tert-Bu 4-[(4-guanidinobenzyl)carbamoyl]-1-piperazinecarboxylate trifluoroacetate underwent deprotection with CF₃CO₂H and amidation with cis-1,5-cyclooctylene chloroformate 4-(tert-butoxycarbonyl)-1-piperazinecarboxylate (77%), followed by a second deprotection and reaction with tert-Bu 4-(2-isocyanatoethyl)-1-piperidinecarboxylate, to give title compd. II. Compds. I inhibited human **tryptase** in vitro with IC₅₀ in the range of 0.0001 to 41 .mu.M.

=> d 17
L7 HAS NO ANSWERS
L7 STR



REP G1=(1-2) CH2
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT IS MCY UNS AT 9
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC 1
NUMBER OF NODES IS 11

STEREO ATTRIBUTES: NONE

=> d 19
L9 HAS NO ANSWERS
L9 SCR 1842

=> d 111
L11 HAS NO ANSWERS
L11 SCR 1841 OR 1840

=> s 17 and 111 not 19
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SAMPLE SCREEN SEARCH COMPLETED - 17257 TO ITERATE

5.8% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 337291 TO 352989
PROJECTED ANSWERS: 0 TO 0

L14 0 SEA SSS SAM L7 AND L11 NOT L9

=>
=> s 17 and 111 not 19 ful
FULL SEARCH INITIATED 15:38:00 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 341711 TO ITERATE

100.0% PROCESSED 341711 ITERATIONS 430 ANSWERS
SEARCH TIME: 00.00.21

L15 430 SEA SSS FUL L7 AND L11 NOT L9

=> fil caplus		SINCE FILE	TOTAL
COST IN U.S. DOLLARS		ENTRY	SESSION
FULL ESTIMATED COST		144.46	144.67

FILE 'CAPLUS' ENTERED AT 15:38:26 ON 03 SEP 2002
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FILE COVERS 1907 - 3 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 2 Sep 2002 (20020902/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s 115
L16 2 L15

=> d bib abs 1-2

L16 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,				

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 PRAI GB 2000-12362 A 20000522
 US 2001-843126 A 20010426
 OS MARPAT 136:5917
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are .beta. to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prep'd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr2NET, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
 AN 1995:545553 CAPLUS
 DN 122:290875
 TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
 IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
 PA Thomae, Dr. Karl, G.m.b.H., Germany
 SO Ger. Offen., 32 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4234295	A1	19940414	DE 1992-4234295	19921012
	EP 592949	A2	19940420	EP 1993-116244	19931007
	EP 592949	A3	19940810		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2108093	AA	19940413	CA 1993-2108093	19931008
	JP 06199788	A2	19940719	JP 1993-252019	19931008
	FI 9304460	A	19940413	FI 1993-4460	19931011
	NO 9303647	A	19940413	NO 1993-3647	19931011
	NO 180232	B	19961202		
	NO 180232	C	19970312		
	AU 9348939	A1	19940428	AU 1993-48939	19931011
	AU 668765	B2	19960516		
	ZA 9307502	A	19950411	ZA 1993-7502	19931011
	CN 1087904	A	19940615	CN 1993-118925	19931012
	US 5442064	A	19950815	US 1993-135041	19931012
PRAI	DE 1992-4234295		19921012		
OS	MARPAT 122:290875				
AB	ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene,				

etc.; D = CH₂, CH₂CH₂, CO, CH₂CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO₂R₅; R₅ = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O₂N)C₆H₄O₂CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC₅₀ of 4.300nM against platelet aggregation in vitro.

=> d hitstr 2

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS

IT 162996-75-0P 162996-88-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as platelet aggregation inhibitors)

RN 162996-75-0 CAPLUS

CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

CH₂ CO₂H

N

C O

N

● HCl

H₂N CH₂

RN 162996-88-5 CAPLUS

CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

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CH₂ C OMe

N

C O

N

● HCl

H₂N CH₂

=> d 11
L1 HAS NO ANSWERS
L1 STR

14

CY 12
C O
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9 N 10
7 C G1
8 C C 11

1 C 2 C C @3

6 C C @4
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REP G1=(1-2) CH
VPA 15-3/4/5 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 4 11
NUMBER OF NODES IS 16

STEREO ATTRIBUTES: NONE

=> s 11 ful
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FULL SCREEN SEARCH COMPLETED - 32670 TO ITERATE

100.0% PROCESSED 32670 ITERATIONS 465 ANSWERS
SEARCH TIME: 00.00.03

L3 465 SEA SSS FUL L1

=> fil caplus
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ENTRY SESSION
FULL ESTIMATED COST 141.80 142.01

FILE 'CAPLUS' ENTERED AT 13:42:21 ON 03 SEP 2002
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American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 3 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 2 Sep 2002 (20020902/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s 13
L4 2 L3

=> d bib abs 1-2

L4 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 2001:868447 CAPLUS
DN 136:5917
TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as tryptase inhibitors
IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian; Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James; Neuenschwander, Kent
PA Aventis Pharmaceuticals Products Inc., USA
SO PCT Int. Appl., 267 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
OS	MARPAT	136:5917			
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring are β . to each other; R1-2 = H, alkyl; R3 = (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.; R4 = H, acyl, alkoxy, alkyloxycarbonyl, carboxy, CN, halo, etc.; n = 0 - 4] were prep'd. Over 300 synthetic examples were disclosed. For instance, 3-bromobenzylbromide was converted in two steps to boronate II. II was

coupled to the triflate ester deriv. of the enol of 4-oxo-N-benzyloxycarbonylpiperidine (DMF, K₂CO₃, PdCl₂(dppf).bul.CH₂Cl₂, 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This intermediate was deprotected and reduced to the piperidine (EtOH, 10% Pd-C/H₂, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic acid (DMF, HAPyU, iPr₂NET, room temp., 18 h) to give III. III had Ki = 50 nM for tryptase. I are useful in the treatment of e.g., asthma and inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1995:546553 CAPLUS
DN 122:290875
TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 32 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4234295	A1	19940414	DE 1992-4234295	19921012
EP 592949	A2	19940420	EP 1993-116244	19931007
EP 592949	A3	19940810		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CA 2108093	AA	19940413	CA 1993-2108093	19931008
JP 06199788	A2	19940719	JP 1993-252019	19931008
FI 9304460	A	19940413	FI 1993-4460	19931011
NO 9303647	A	19940413	NO 1993-3647	19931011
NO 180232	B	19961202		
NO 180232	C	19970312		
AU 9348939	A1	19940428	AU 1993-48939	19931011
AU 668755	B2	19960516		
ZA 9307502	A	19950411	ZA 1993-7502	19931011
CN 1087904	A	19940615	CN 1993-118925	19931012
US 5442064	A	19950815	US 1993-135041	19931012

PRAI DE 1992-4234295 19921012
OS MARPAT 122:290875
AB ABCDEFG [A = amino(alkyl), C(:NH)NH₂, NHC(:NH)NH₂, etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene, etc.; D = CH₂, CH₂CH₂, CO, CH₂CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO₂R₅; R₅ = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O₂N)C₆H₄O₂CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC₅₀ of 4.300nM against platelet aggregation in vitro.

=> d hitstr 2

L4 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
IT 162996-75-0P 162996-88-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as

platelet aggregation inhibitors)
RN 162996-75-0 CAPLUS
CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)

CH₂ CO₂H

N

C O

N ● HCl

H₂N CH₂

RN 162996-88-5 CAPLUS
CN 4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

O

CH₂ C OMe

N

C O

N ● HCl

H₂N CH₂

AN 2002:675993 CAPLUS
 DN 137:216874
 TI Acylated piperidine derivatives, specifically 1-(pyrrolidinylcarbonyl)piperidines, 1-(piperidinylcarbonyl)piperidines, and analogs, as melanocortin-4 receptor agonists, and their pharmaceutical compositions and therapeutic uses
 IN Ujjainwalla, Feroze; Chu, Lin; Goulet, Mark T.; Lee, Bonnie; Warner, Daniel; Wyvratt, Matthew J.
 PA Merck & Co., Inc., USA
 SO PCT Int. Appl., 112 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002068388	A2	20020906	WO 2002-US5724	20020225
	WO 2002068388	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRAI	US 2001-272258P	P	20010228		
	US 2001-300118P	P	20010622		
OS	MARPAT 137:216874				
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Certain novel 4-substituted N-acylated piperidine derivs., specifically I, are agonists of the human melanocortin receptor(s) and, in particular, are selective agonists of the human melanocortin-4 receptor (MC-4R) [wherein: p = 1 or 2; q = 0, 1, or 2; n = 0, 1, or 2; R1 = H, amidino, alkyliminoyl, (un)substituted alkyl, (CH₂)_n-G1 [G1 = (un)substituted cycloalkyl, Ph, naphthyl, or heteroaryl]; R2 = (un)substituted Ph, naphthyl, or heteroaryl; X = alkyl, (CH₂)_n-G2 [G2 = (un)substituted cycloalkyl, Ph, naphthyl, heteroaryl, heterocyclyl, cyano, CONH₂, CO₂H, OH, NH₂, and various derivs.] where any of (CH₂)_n may also be substituted; including pharmaceutically acceptable salts]. They are therefore useful for the treatment, control, or prevention of diseases and disorders responsive to the activation of MC-4R, such as obesity, diabetes, sexual dysfunction, including erectile dysfunction and female sexual dysfunction. Approx. 180 invention compds. I and approx. 25 intermediates were prep'd. For instance, (2-bromo-5-chlorophenyl)acetic acid underwent a sequence of Me esterification, coupling with tert-Bu 4-[[[trifluoromethyl)sulfonyl]oxy]-3,6-dihydropyridine-1(2H)-carboxylate via a boronate ester, removal of the BOC group, and amidation with (3S,4R)-1-(tert-butyl)-4-(2,4-difluorophenyl)pyrrolidine-3-carboxylic acid. The unsatd. amide-ester underwent hydrogenation, sapon. of the ester, and amidation with MeNH₂.HCl, to give title compd. II. Representative compds. I bound to cloned human MC-4R in vitro with IC₅₀ values generally below 2 .mu.M, and also acted as agonists toward cloned human MCR in a functional assay with EC₅₀ values less than 1 .mu.M.

IT 455957-91-2P, tert-Butyl 4-[2-((1S)-1-aminoethyl)-4-

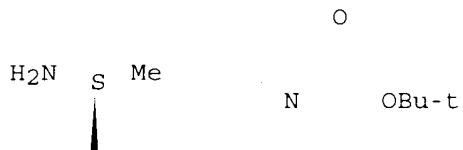
chlorophenyl]piperidine-1-carboxylate **455957-92-3p**, tert-Butyl
4-[2-[(1S)-1-(acetylamino)ethyl]-4-chlorophenyl]piperidine-1-carboxylate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)

(intermediate; prepn. of acylated piperidine derivs., particularly
(pyrrolidinylcarbonyl)piperidines, (piperidinylcarbonyl)piperidines,
and analogs, as melanocortin-4 receptor agonists)

RN 455957-91-2 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[2-[(1S)-1-aminoethyl]-4-chlorophenyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

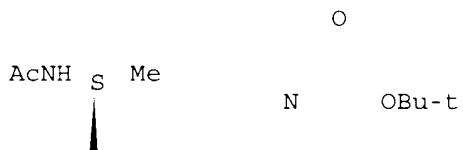


C1

RN 455957-92-3 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[2-[(1S)-1-(acetylamino)ethyl]-4-
chlorophenyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



C1

AN 1995:546553 CAPLUS
 DN 122:290875
 TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors
 IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard;
 Mueller, Thomas; Weisenberger, Johannes; Guth, Brian
 PA Thomae, Dr. Karl, G.m.b.H., Germany
 SO Ger. Offen., 32 pp.
 CODEN: GWXXBX
 DT Patent
 LA German
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4234295	A1	19940414	DE 1992-4234295	19921012
	EP 592949	A2	19940420	EP 1993-116244	19931007
	EP 592949	A3	19940810		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2108093	AA	19940413	CA 1993-2108093	19931008
	JP 06199788	A2	19940719	JP 1993-252019	19931008
	FI 9304460	A	19940413	FI 1993-4460	19931011
	NO 9303647	A	19940413	NO 1993-3647	19931011
	NO 180232	B	19961202		
	NO 180232	C	19970312		
	AU 9348939	A1	19940428	AU 1993-48939	19931011
	AU 668765	B2	19960516		
	ZA 9307502	A	19950411	ZA 1993-7502	19931011
	CN 1087904	A	19940615	CN 1993-118925	19931012
	US 5442064	A	19950815	US 1993-135041	19931012
PRAI	DE 1992-4234295		19921012		
OS	MARPAT 122:290875				
AB	ABCDEF [A = amino(alkyl), C(:NH)NH ₂ , NHC(:NH)NH ₂ , etc.; B = (un)substituted (di)azinylene; C = 1,4-cyclohexylene, 1,4-piperidinylene, etc.; D = CH ₂ , CH ₂ CH ₂ , CO, CH ₂ CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylene, etc.; F = alkylene, bond(E .noteq. piperazinylene); G = CO ₂ R ₅ ; R ₅ = H, alkyl, etc.] were prepd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O ₂ N)C ₆ H ₄ O ₂ CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC ₅₀ of 4.300nM against platelet aggregation in vitro.				
IT	162996-75-0P 162996-87-4P 162996-88-5P				
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
	(prepn. of (di)azine-contg. cyclohexanecarboxylates and analogs as platelet aggregation inhibitors)				
RN	162996-75-0 CAPLUS				
CN	4-Piperidineacetic acid, 1-[[4-[4-(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, monohydrochloride (9CI) (CA INDEX NAME)				

CH₂ CO₂H

N

C O

N

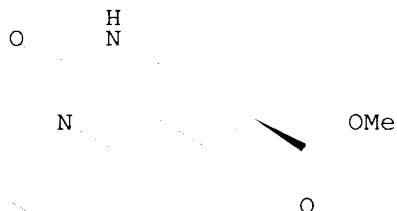
● HCl

H₂N CH₂

RN 162996-87-4 CAPLUS

CN Cyclohexanecarboxylic acid, 4-[[4-[(aminomethyl)phenyl]-1-piperidinyl]carbonyl]amino]-, methyl ester, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



H₂N

● HCl

RN 162996-88-5 CAPLUS

CN 4-Piperidineacetic acid, 1-[[4-[(aminomethyl)phenyl]-1-piperidinyl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

O

CH₂ C OMe

N

C O

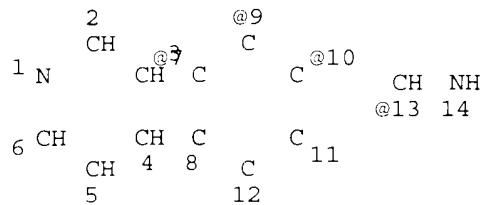
N

● HCl

H₂N CH₂

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L2 STR



VPA 13-7/9/10 U

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DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 10 4

NUMBER OF NODES IS 14

STEREO ATTRIBUTES: NONE

=> s 12

SAMPLE SEARCH INITIATED 16:30:29 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 9815 TO ITERATE

10.2% PROCESSED 1000 ITERATIONS

5 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 190370 TO 202230

PROJECTED ANSWERS: 561 TO 1401

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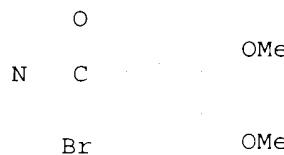
=> d scan

L3 5 ANSWERS REGISTRY COPYRIGHT 2002 ACS

IN Piperidine, 4-[3-(aminomethyl)phenyl]-1-(2-bromo-4,5-dimethoxybenzoyl)-
(9CI)

MF C21 H25 Br N2 O3

CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

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C          C
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          CH  NH
          @13 14
6 CH      CH  C      C 11
      CH  4   8   C 12
      5

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VPA 13-7/9/10 U
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED
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GRAPH ATTRIBUTES:
RSPEC 10 4
NUMBER OF NODES IS 14
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STEREO ATTRIBUTES: NONE
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FULL SCREEN SEARCH COMPLETED - 198064 TO ITERATE
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100.0% PROCESSED 198064 ITERATIONS          666 ANSWERS
SEARCH TIME: 00.00.04
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COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                                ENTRY          SESSION
FULL ESTIMATED COST          142.18          142.39
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FILE 'CAPLUS' ENTERED AT 16:30:57 ON 04 SEP 2002
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FILE COVERS 1907 - 4 Sep 2002 VOL 137 ISS 10
FILE LAST UPDATED: 3 Sep 2002 (20020903/ED)
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This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For

information on CAS roles, enter HELP ROLES at an arrow prompt or use
the CAS Roles thesaurus (/RL field) in this file.

=> S 14
L5 8 L4

L5 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2002 ACS
 AN 2001:868447 CAPLUS
 DN 136:5917
 TI Preparation of (hetero)arylacyl-piperidinyl-benzylamines for use as
 tryptase inhibitors
 IN Astles, Peter C.; Eastwood, Paul R.; Houille, Olivier; Levell, Julian;
 Pauls, Heinz; Czekaj, Mark; Liang, Guyan; Gong, Yong; Pribish, James;
 Neuenschwander, Kent
 PA Aventis Pharmaceuticals Products Inc., USA
 SO PCT Int. Appl., 267 pp.
 CODEN: PIKXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001090101	A1	20011129	WO 2001-US13811	20010427
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRAI	GB 2000-12362	A	20000522		
	US 2001-843126	A	20010426		
OS	MARPAT	136:5917			
GI					

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [Ar = (hetero)aryl, where the two groups on the Ar ring
 are .beta. to each other; R1-2 = H, alkyl; R3 =
 (un)substituted(hetero)aryl, arylalkenyl, cycloalkenyl, cycloalkyl, etc.;
 R4 = H, acyl, alkoxy, alkylloxycarbonyl, carboxy, CN, halo, etc.; n = 0 -
 4] were prep'd. Over 300 synthetic examples were disclosed. For instance,
 3-bromobenzylbromide was converted in two steps to boronate II. II was
 coupled to the triflate ester deriv. of the enol of 4-oxo-N-
 benzylloxycarbonylpiperidine (DMF, K2CO3, PdCl2(dppf).bul.CH2Cl2,
 80.degree.C, 18 h) to give the corresponding bicyclic intermediate. This
 intermediate was deprotected and reduced to the piperidine (EtOH, 10%
 Pd-C/H2, room temp., 5 h) and coupled to 5-phenethylthiophene-2-carboxylic
 acid (DMF, HApYU, iPr2NET, room temp., 18 h) to give III. III had Ki = 50
 nM for tryptase. I are useful in the treatment of e.g., asthma and
 inflammatory diseases.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2002 ACS
 AN 1999:348249 CAPLUS
 DN 131:102177
 TI Substituted piperidines - highly potent renin inhibitors due to induced
 fit adaptation of the active site
 AU Vieira, Eric; Binggeli, Alfred; Breu, Volker; Bur, Daniel; Fischli,
 Walter; Guller, Rolf; Hirth, Georges; Marki, Hans Peter; Muller, Marcel;
 Oefner, Christian; Scalzone, Michelangelo; Stadler, Heinz; Wilhelm,
 Maurice; Wostl, Wolfgang

CS Pharma Research Departments, F. Hoffmann-La Roche Ltd, Basel, CH-4070,
Switz.
SO Bioorganic & Medicinal Chemistry Letters (1999), 9(10), 1397-1402
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
GI

H
N

OCH₂

O(CH₂)₃OCH₂Ph

I

AB The identification, synthesis and activity of a novel class of piperidine renin inhibitors, e.g., I, is presented. The most active compds. show activities in the picomolar range and are among the most potent renin inhibitors ever identified.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1999:191411 CAPLUS
DN 130:242312
TI Pharmaceutical preparations containing piperidine derivatives as antimalarials
IN Bur, Daniel; Fischli, Walter; Matile, Hugues; Ridley, Robert George; Wostl, Wolfgang
PA F.Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9912532	A2	19990318	WO 1998-EP5570	19980902
	WO 9912532	A3	19990729		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9897409	A1	19990329	AU 1998-97409	19980902
PRAI	EP 1997-115510		19970908		
	WO 1998-EP5570		19980902		
AB	Pharmaceutical preps. contg. piperidine derivs. are used against chloroquine-sensitive and chloroquine-resistant pathogens and in the prodn. of corresponding medicaments; furthermore corresponding medicaments				

and a method of treating malaria in a patient in need of such treatment comprises administering to said patient an effective amt. of a corresponding compd. or medicament. The IC50 of (3RS,4RS)-3-(naphthalen-2-ylmethoxy)-4-[4-(2-phenoxy-ethoxy)-phenyl]-piperidine (I) against chloroquine-resistant strains of *Plasmodium falciparum* was 0.6 .mu.M. A tablet contained I 500, lactose 149, PVP 15, dioctyl sodium sulfosuccinate 1, sodium carboxymethyl starch 30, and magnesium stearate 5 mg.

L5 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2002 ACS
 AN 1998:180759 CAPLUS
 DN 128:243953
 TI Preparation of N-aralkylpyridine-4-amines and analogs as thrombin inhibitors
 IN Naylor-Olsen, Adel M.; Ponticello, Gerald S.; Vacca, Joseph P.; Hungate, Randall W.; Coburn, Craig; Phillips, Brian T.; Lewis, S. D.; Fraley, Mark E.
 PA Merck & Co., Inc., USA; Naylor-Olsen, Adel M.; Ponticello, Gerald S.; Vacca, Joseph P.; Hungate, Randall W.; Coburn, Craig; Phillips, Brian T.; Lewis, S. D.; Fraley, Mark E.
 SO PCT Int. Appl., 152 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9810763	A1	19980319	WO 1997-US15989	19970909
	W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9744117	A1	19980402	AU 1997-44117	19970909
	AU 725403	B2	20001012		
	EP 927035	A1	19990707	EP 1997-942415	19970909
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRAI	JP 2001500864	T2	20010123	JP 1998-513809	19970909
	US 1996-26033P	P	19960913		
	GB 1996-24278	A	19961122		
	WO 1997-US15989	W	19970909		
OS	MARPAT 128:243953				
AB	R1CHR2Z1Z2Z3R [I; R = 4-pyridyl, 4-amidino-1-piperazinyl, 4-aminopyridinium-1-yl, 6-amino- or amidino-3-pyridyl, C6H4[C(:NH)NH2]-4; R1,R2 = H, (hetero)aryl, (di)arylalkyl, CONH2, etc.; R1R2 = alkylene; Z1 = O, SOO-2, (alkyl)imino, etc.; Z2 = (un)substituted phenylene; Z3 = (CH2)m, (CH2)mNH, SO2NH, SO2(CH2)m, SO2, (CH2)mSO2; m = 1 or 2] were prep'd. Thus, 4-(PhO)C6H4CO2H was amidated by 4-aminopyridine and the product reduced to give 4-(PhO)C6H4CH2NHR (R = 4-pyridyl). Data for biol. activity of I were given.				

L5 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2002 ACS
 AN 1997:307688 CAPLUS
 DN 126:277402
 TI New 4-aryl-3-aralkoxypiperidines and -azabicylooctanes for treating heart and kidney insufficiency
 IN Binggeli, Alfred; Breu, Volker; Bur, Daniel; Fischli, Walter; Gueller, Rolf; Hirth, Georges; Maerki, Hans-Peter; Mueller, Marcel; Oefner, Christian; Stadler, Heinz; Vieira, Eric; Wilhelm, Maurice; Wostl, Wolfgang F. Hoffmann-La Roche Ag, Switz.
 PA PCT Int. Appl., 492 pp.
 SO CODEN: PIXXD2

DT Patent
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9709311	A1	19970313	WO 1996-EP3803	19960829
	W: AU, BR, CA, CN, CZ, HU, IL, JP, KR, MX, NO, NZ, PL, RU, SG, TR RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	CA 2230931	AA	19970313	CA 1996-2230931	19960829
	AU 9667432	A1	19970327	AU 1996-67432	19960829
	AU 708616	B2	19990805		
	EP 863875	A1	19980916	EP 1996-927715	19960829
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	CN 1202152	A	19981216	CN 1996-197674	19960829
	JP 11500447	T2	19990112	JP 1996-510837	19960829
	BR 9610385	A	19990706	BR 1996-10385	19960829
	RU 2167865	C2	20010527	RU 1998-106388	19960829
	ZA 9607424	A	19970307	ZA 1996-7424	19960902
	NO 9800954	A	19980428	NO 1998-954	19980305
	US 6051712	A	20000418	US 1999-255185	19990222
	US 6150526	A	20001121	US 1999-456283	19991207
PRAI	CH 1995-2548	A	19950907		
	CH 1996-1876	A	19960726		
	WO 1996-EP3803	W	19960829		
	US 1996-711339	A3	19960906		
	US 1999-255185	A1	19990222		
OS	MARPAT 126:277402				
GI					

F

CH₂O

Pr

N
H

OCH₂Ph

I

AB New piperidine and azabicyclooctane derivs. (> 1000 compds.) are renin inhibitors for treatment of high blood pressure, heart and kidney insufficiency. Thus, the piperidine deriv. I was prep'd. from 1-benzyl-3-propyl-4-piperidinone by reaction with 4-FC₆H₄Br, followed by 1-benzyloxy-3-chloromethylnaphthalene and deblocking. I had a renin-inhibiting IC₅₀ of 0.317 .mu.M.

L5 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2002 ACS
AN 1995:546553 CAPLUS

DN 122:290875

TI Preparation of (di)azine-containing cyclohexanecarboxylates and analogs as platelet aggregation inhibitors

IN Pieper, Helmut; Linz, Guenter; Himmelsbach, Frank; Austel, Volkhard; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian

PA Thomae, Dr. Karl, G.m.b.H., Germany
SO Ger. Offen., 32 pp.
CODEN: GWXXBX

DT Patent
LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4234295	A1	19940414	DE 1992-4234295	19921012
	EP 592949	A2	19940420	EP 1993-116244	19931007
	EP 592949	A3	19940810		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	CA 2108093	AA	19940413	CA 1993-2108093	19931008
	JP 06199788	A2	19940719	JP 1993-252019	19931008
	FI 9304460	A	19940413	FI 1993-4460	19931011
	NO 9303647	A	19940413	NO 1993-3647	19931011
	NO 180232	B	19961202		
	NO 180232	C	19970312		
	AU 9348939	A1	19940428	AU 1993-48939	19931011
	AU 668765	B2	19960516		
	ZA 9307502	A	19950411	ZA 1993-7502	19931011
	CN 1087904	A	19940615	CN 1993-118925	19931012
	US 5442064	A	19950815	US 1993-135041	19931012
PRAI	DE 1992-4234295		19921012		
OS	MARPAT 122:290875				

AB ABCDEFG [A = amino(alkyl), C(:NH)NH2, NHC(:NH)NH2, etc.; B = (un)substituted (di)azinylen; C = 1,4-cyclohexylene, 1,4-piperidinylen, etc.; D = CH2, CH2CH2, CO, CH2CO; E = 1,4-cyclohex(en)ylene, 1,4-piperidinylen, etc.; F = alkylene, bond(E .noteq. piperazinylen); G = CO2R5; R5 = H, alkyl, etc.] were prepnd. Thus, Me trans-4-aminocyclohexanecarboxylate was amidated by 4-(O2N)C6H4O2CCl and the product condensed with 1-(4-cyanophenyl)piperazine (prepn. given) to give, after hydrogenation, 1-(4-aminophenyl)-[N-[trans-4-(methoxycarbonyl)cyclohexyl]aminocarbonyl]piperazine hydrochloride which had IC50 of 4.300nM against platelet aggregation in vitro.

L5 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1994:533976 CAPLUS

DN 121:133976

TI Carboxylic Acid Derivatives and Their Uses as Pharmaceuticals

IN Himmelsbach, Frank; Linz, Guenter; Austel, Volkhard; Pieper, Helmut; Mueller, Thomas; Weisenberger, Johannes; Guth, Brian

PA Thomae, Dr. Karl, G.m.b.H., Germany

SO Ger. Offen., 24 pp.

CODEN: GWXXBX

DT Patent

LA German

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 4241632	A1	19940616	DE 1992-4241632	19921210
	CA 2111035	AA	19940611	CA 1993-2111035	19931208
	EP 604800	A1	19940706	EP 1993-119786	19931208
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	FI 9305513	A	19940611	FI 1993-5513	19931209
	NO 9304501	A	19940613	NO 1993-4501	19931209
	JP 06239817	A2	19940830	JP 1993-308419	19931209
	ZA 9309230	A	19950609	ZA 1993-9230	19931209
	AU 9352306	A1	19940623	AU 1993-52306	19931210
	CN 1094035	A	19941026	CN 1993-120876	19931210
PRAI	DE 1992-4241632		19921210		
OS	MARPAT 121:133976				

GI

OMe

O NH

HN

O I

AB Pharmacol. active carboxylates were disclosed. A specifically claimed example compd., Me trans-4-[[4-(4-piperidinyl)phenyl]carbonylamino]cyclohexanepropanoate (I) was prep'd. The claimed compds. are blood platelet aggregation inhibitors (antithrombotics).

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS

AN 1992:235449 CAPLUS

DN 116:235449

TI Piperidine compounds, their preparation and use
IN Jakobsen, Palle; Kanstrup, Anders; Lundbeck, Jane Marie

PA Novo-Nordisk A/S, Den.

SO PCT Int. Appl., 60 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9201672	A1	19920206	WO 1991-DK206	19910715
	W: AU, CA, CS, FI, HU, JP, KR, NO, PL				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
	IL 98757	A1	19970110	IL 1991-98757	19910708
	AU 9182241	A1	19920218	AU 1991-82241	19910715
	AU 661276	B2	19950720		
	EP 558487	A1	19930908	EP 1991-913359	19910715
	EP 558487	B1	19981007		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	JP 06500076	T2	19940106	JP 1991-512512	19910715
	AT 171943	E	19981015	AT 1991-913359	19910715
	CN 1058207	A	19920129	CN 1991-104954	19910718
	ZA 9105647	A	19920527	ZA 1991-5647	19910718
	NO 9300143	A	19930118	NO 1993-143	19930115
	NO 179974	B	19961014		
	NO 179974	C	19970122		
	US 5328917	A	19940712	US 1993-65513	19930520
PRAI	DK 1990-1724		19900718		
	DK 1991-117		19910124		
	US 1991-728930		19910712		
	WO 1991-DK206		19910715		
OS	MARPAT	116:235449			
GI					

CH₂Y(CH₂)_nR³

X

NR¹

I

AB Title compds. I (R¹ = H, C1-8 alkyl, C1-8 alkyl, C1-8-alkoxy-C1-8-alkyl, C3-8 cycloalkyl, C2-6 alkenyl, C4-8 cycloalkylalkyl, Ac, C2-6 alkynyl; R³ = 3,4-methylenedioxyphenyl, (substituted) Ph naphthyl, (substituted) 5-, 6-membered heterocycl contg. 1 or 2 N, O, S X = H₂N, O₂N, mono-, dialkylamino, HO₂C, alkanoylamino, etc.; Y = O, S, RN whereas R = H, C1-5 alkyl; n = 0-4) or a salt thereof, useful in treatment of Ca overload, are prep'd. 3-[(Benzenesulfonyloxy)methyl]-1-butyl-4-phenylpiperidine was mixed with 4-(MeO)C₆H₄CH₂NH₂ and heated for 4 h at 90.degree. to give I (R¹ = Bu, R³ = 4-(MeO)C₆H₄, X = H, Y = HN, n = 1) (II). II showed an inhibition of Ca uptake in brain synaptosomes, IC₅₀ of 2.7 .mu.g/mL, vs. diltiazem 96 .mu.g/mL. A tablet formulation comprising I is given.

=> d hitstr 8

L5 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2002 ACS

IT **141360-48-7P**

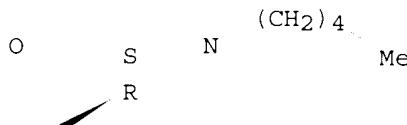
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of, as calcium antagonist)

RN 141360-48-7 CAPLUS

CN Benzenemethanamine, 4-[(1-pentyl-3-[[4-(trifluoromethyl)phenoxy]methyl]-4-piperidinyl)-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

F₃C



H₂N

● HCl

AN 2000:243073 CAPLUS
DN 132:246060
TI Effects of fluticasone propionate on tryptase serum levels in allergic rhinitis
AU Bruno, G.; Andreozzi, P.; Magrini, L.; Zaino, S.; Graf, U.
CS Istituto di I Clinica Medica, Fondazione A. Cesalpino Universita La Sapienza, Rome, Italy
SO World Congress of Asthma, 16th, Buenos Aires, Argentina, Oct. 17-20, 1999 (1999), 121-124. Editor(s): Neffen, Hugo E.; Baena-Cagnani, Carlos E.; Yanez, Anahi. Publisher: Monduzzi Editore, Bologna, Italy.
CODEN: 68UFA9
DT Conference
LA English
AB In allergic rhinitis (AR) such as in other allergic reactions, studies draw attention to the potential of neutral proteases, proteoglycans, eicosanoids and various cytokines that are released by mast cells. Among these mediators, **tryptase** is known to be a specific marker of mast cell activation. This study was devoted to evaluate the serum **tryptase** in AR and the effect of fluticasone propionate (Ftp) on serum levels of this mediator. The basal values of **tryptase** (M.+-SD: 6.1.+-2.4 .mu.g/L) resulted to be significantly (p < 0.02) higher in 13 AR subjects than in the controls (3.0.+-1.2 .mu.g/L). **Tryptase** values decreased significantly (p < 0.04) after 15 days of 100 .mu.g of Ftp treatment (M.+-SD: 4.5.+-3.1 .mu.g/L) which was administered twice a day. After two weeks of wash-out, **tryptase** values (M.+-SD: 5.5.+-2.6 .mu.g/L) increased again significantly (p < 0.05). The intranasal **corticosteroids** are effective in modulating the mucosal inflammation of AR, leading also to a decrease of mast cell activation.

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT